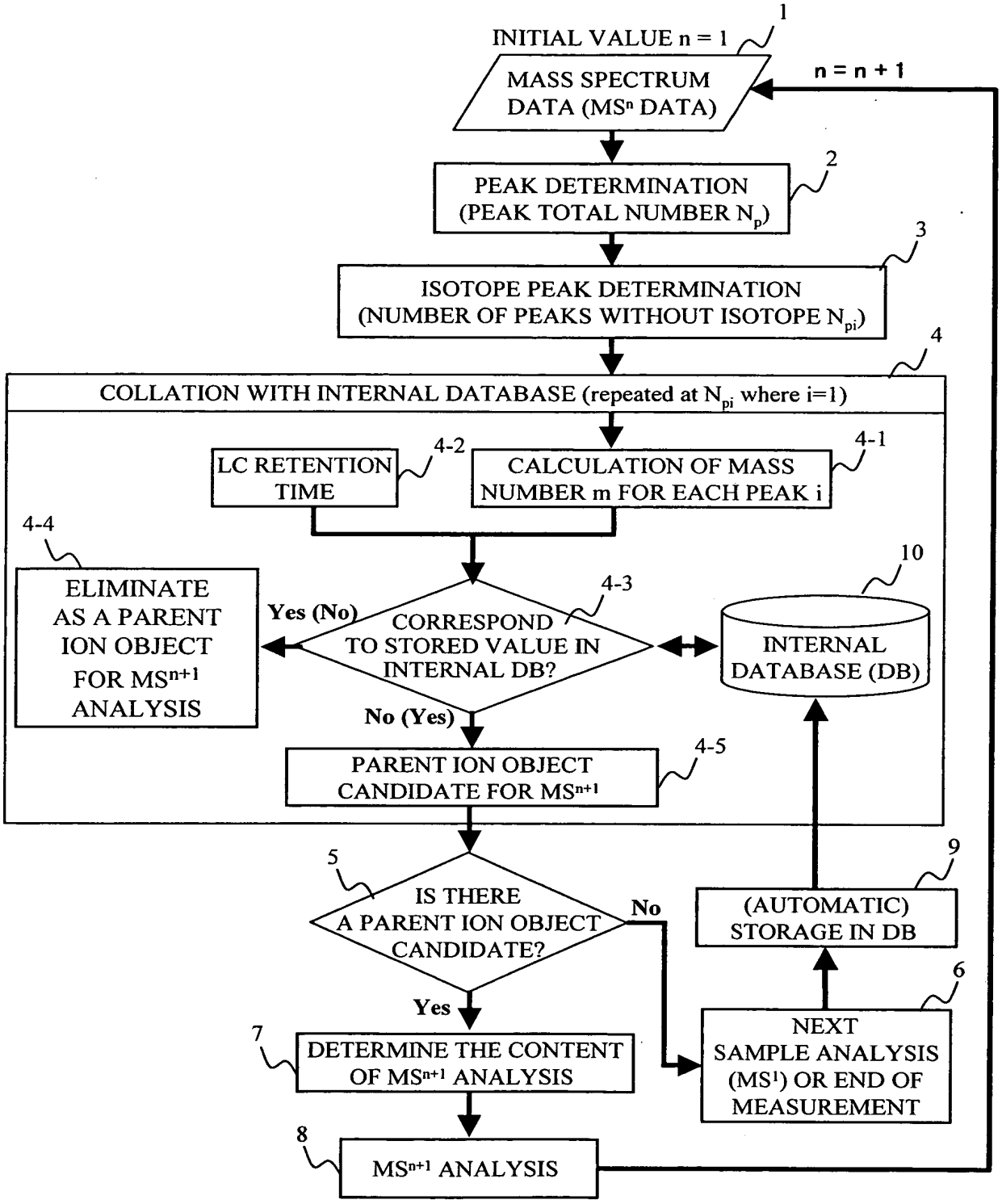
OIPE
SEP 17 2004
PATENT & TRADEMARK OFFICE

FIG. 1



BEST AVAILABLE COPY

FIG. 2

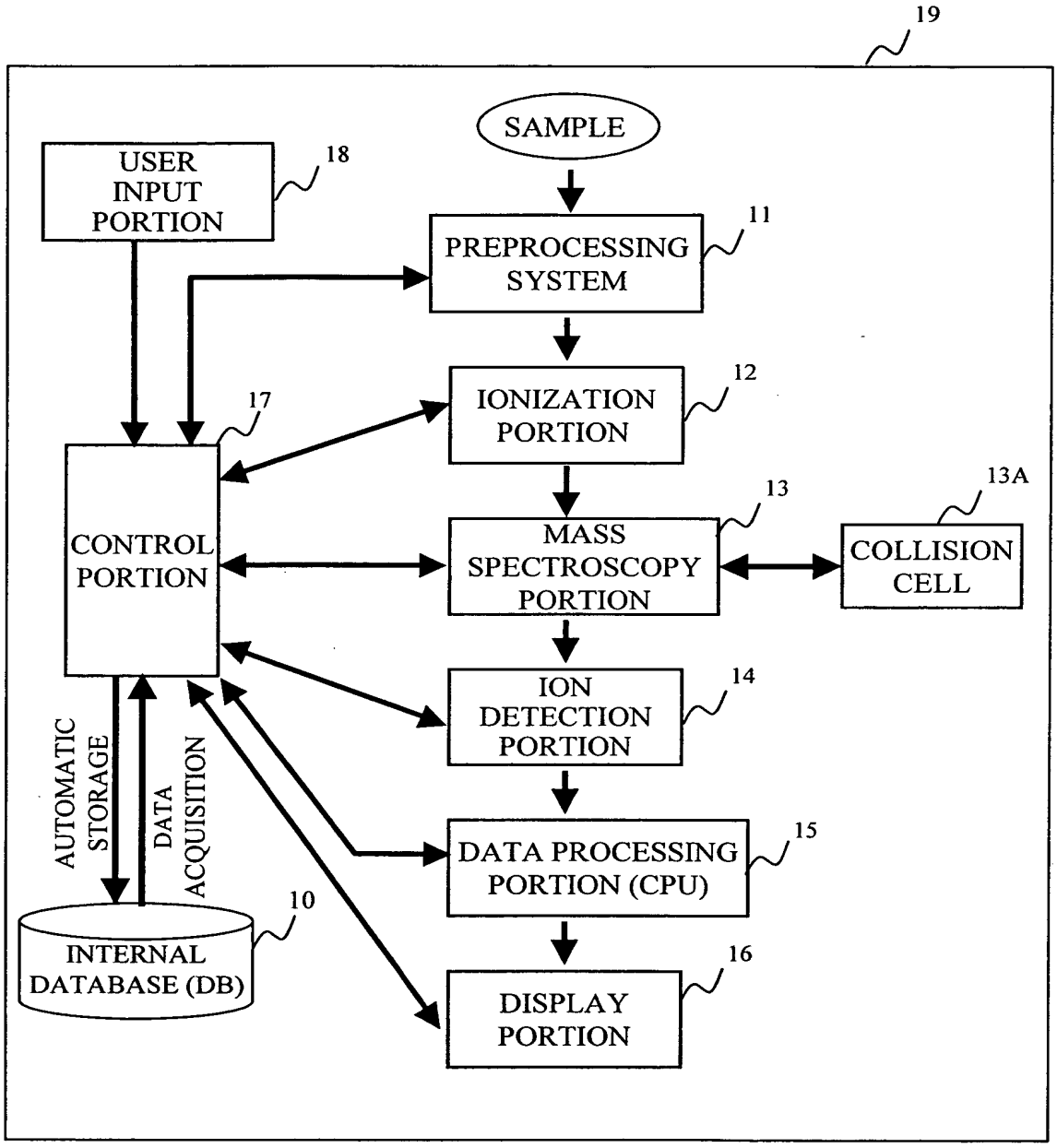

19
SAMPLE
USER INPUT PORTION
18
PREPROCESSING SYSTEM
11
IONIZATION PORTION
12
17
CONTROL PORTION
MASS SPECTROSCOPY PORTION
13
13A
COLLISION CELL
ION DETECTION PORTION
14
AUTOMATIC STORAGE
DATA ACQUISITION
DATA PROCESSING PORTION (CPU)
15
INTERNAL DATABASE (DB)
10
DISPLAY PORTION
16

FIG. 3 A

PRIOR ART METHOD

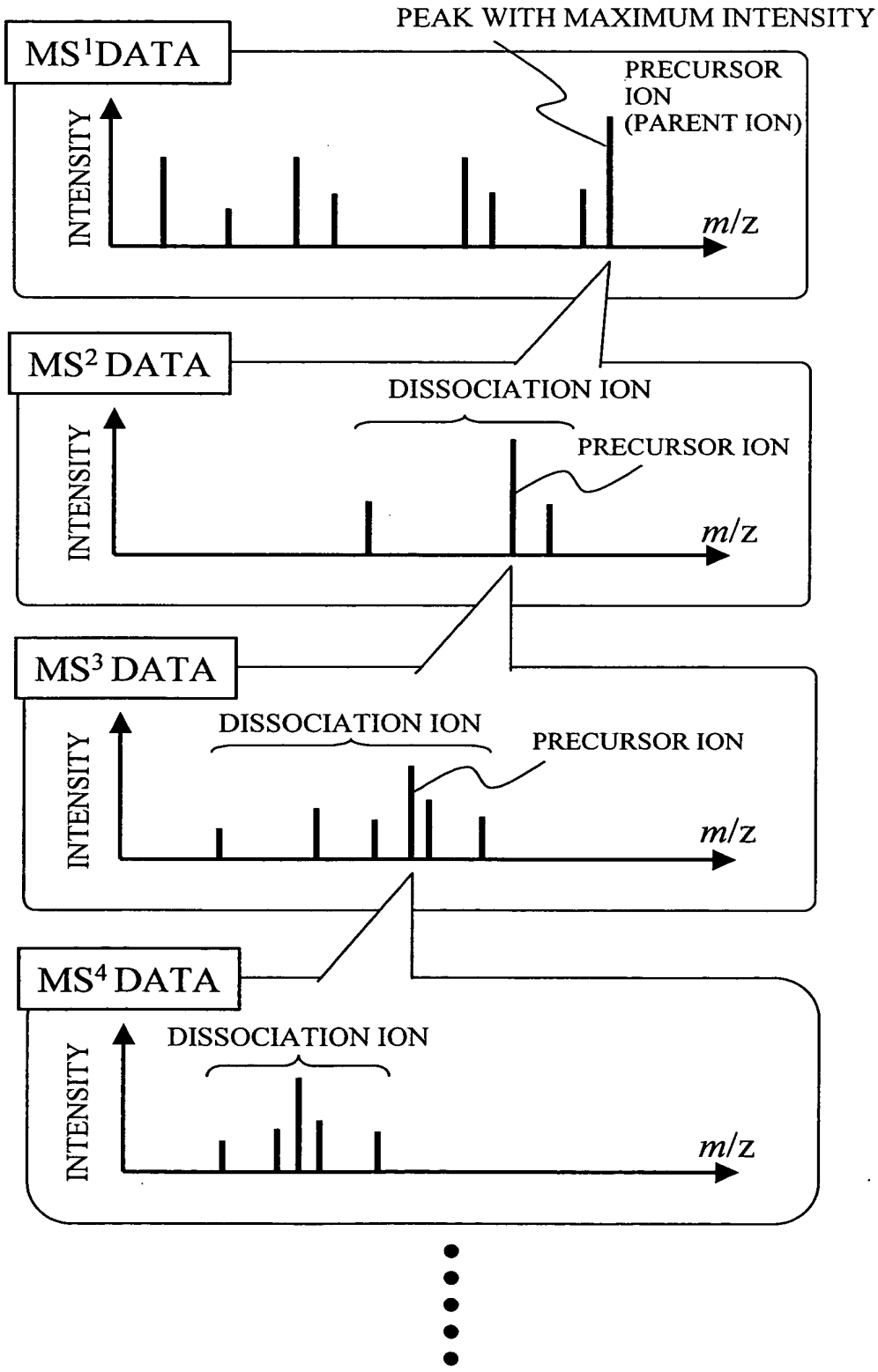


FIG. 3 B

EMBODIMENT 1

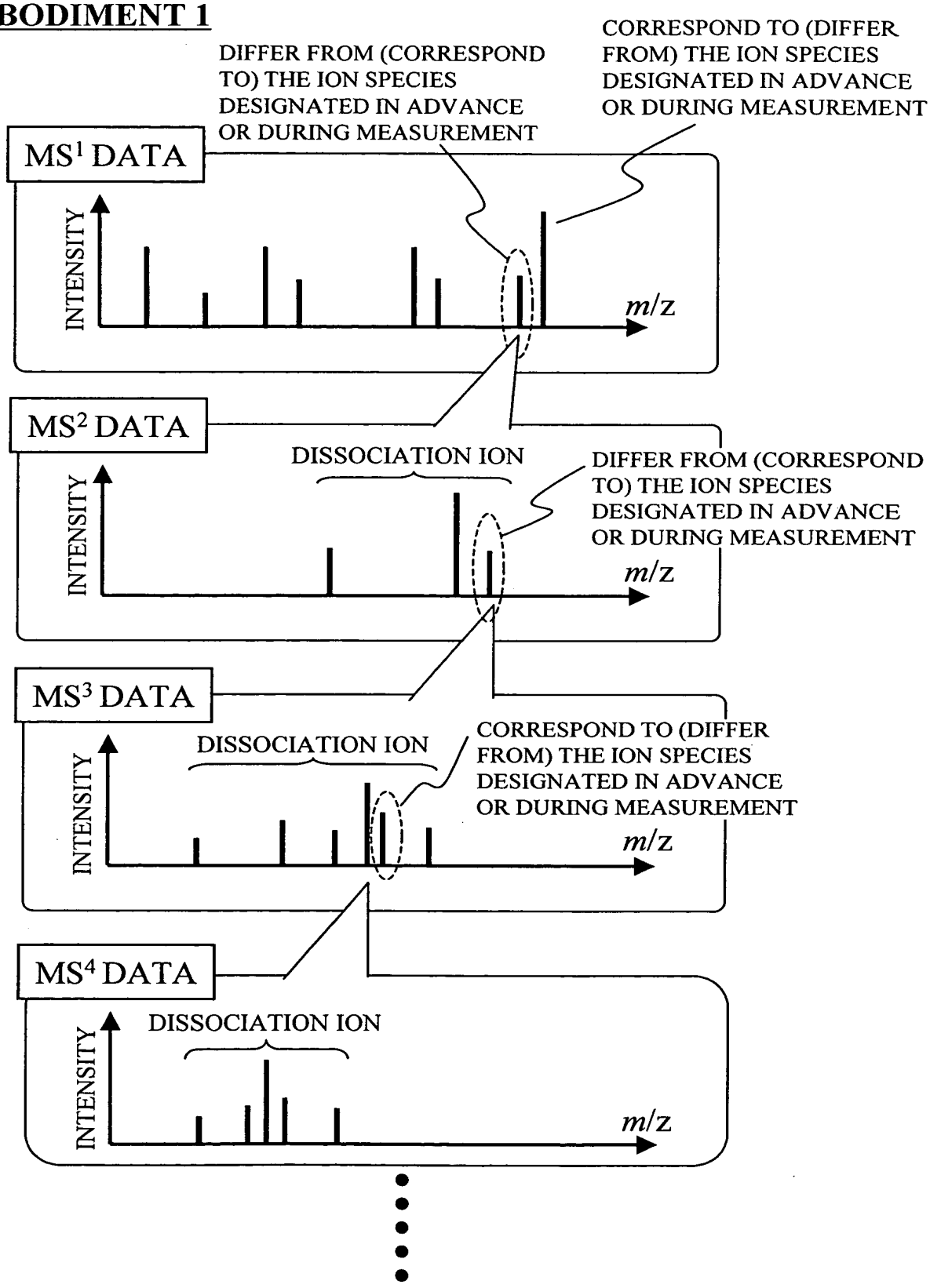


FIG. 3 C

EMBODIMENT 2

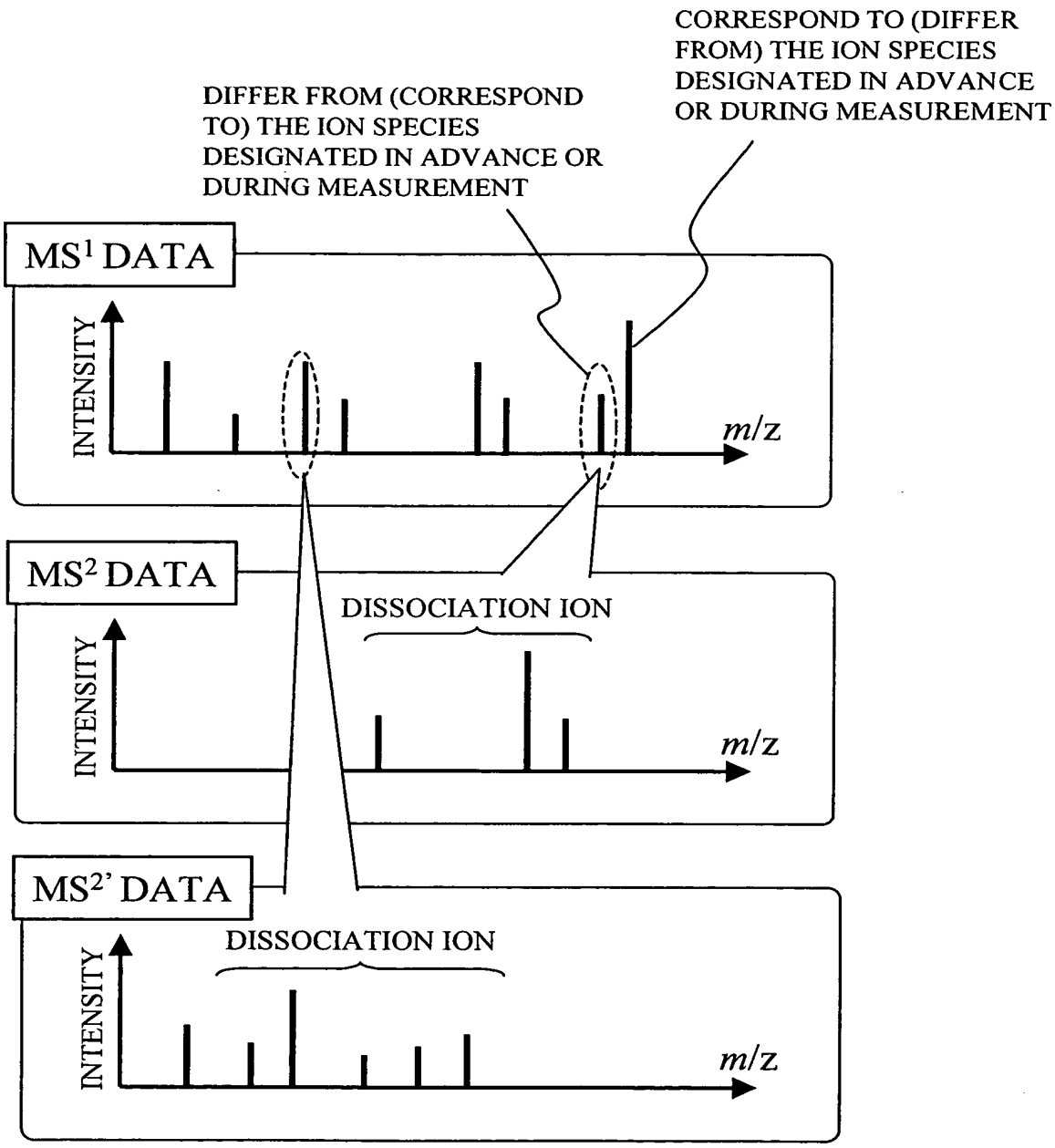
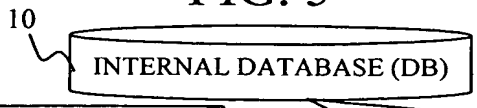


FIG. 4


9
(AUTOMATIC) STORAGE IN DB
AMINO ACID SEQUENCE OF IDENTIFIED PROTEIN A
IN THE CASE OF HUMAN MYOGLOBIN
N TERMINAL--- MGLSDGEWQLVLNVWGKVEADIPGHGQEVLIRLFKGHPETLEKFDKFKH---
---LKSEDEMKASEDLKKHGATVLTALGGIL KKKGHHEAEIKPLAQSHATKHKIPVK---
---YLEFISECIIQVLQSKHPGDFGADAQGAMNKALELFRKDMASNYKELGFQG --- C TERMINAL
TYPES OF DIGESTIVE ENZYME
(EXAMPLE) TRYPSIN
FEATURE OF CLEAVAGE C TERMINAL IS R OR K
SEQUENCE AND MASS NUMBER OF PEPTIDE EXPECTED TO BE PRODUCED AFTER ENZYMATIC DIGESTION
EXPECTED PRODUCED PEPTIDE
AMINO ACID SEQUENCE
MASS NUMBER M [Da]
PEPTIDE A MGLSDGEWQLVLNVWGK 1932.20484
PEPTIDE B VEADIPGHGQEVLIR 1632.81642
PEPTIDE C LFK 406.519220
PEPTIDE D GHPETLEK 909.983260
PEPTIDE E FDK 408.448980
PEPTIDE F FK 293.361540
PEPTIDE G HLK 396.484720
PEPTIDE H SEDEMK 737.777560
PEPTIDE I ASEDLK 661.702060
PEPTIDE J K 146.187640
PEPTIDE K HGATVLTALGGILK 1350.60666
PEPTIDE L K 146.187640
PEPTIDE M K 146.187640
PEPTIDE N GHHEAEIK PLAQSHATK 1854.048
PEPTIDE O HK 283.327040
PEPTIDE P IPVK 455.591640
PEPTIDE Q YLEFISECIIQVLQSK 1913.23960
PEPTIDE R HPGDFGADAQGAMNK 1515.60806
PEPTIDE S ALELFR 747.882340
PEPTIDE T K 146.187640
PEPTIDE U DMASNYK 827.903480
PEPTIDE V ELGFQG 649.692900
* SINGLE-LETTER NOTATION OF AMINO ACIDS
(AUTOMATIC) STORAGE IN INTERNAL DATABASE

FIG. 5



CONTENT OF THE INTERNAL DATABASE

• CHARACTERISTICS DATA OF A PEPTIDE THAT HAS ONCE BEEN SUBJECTED TO MS^n ($n \geq 2$) MEASUREMENT
(MASS NUMBER m, RETENTION TIME IN LC τ, VALENCE z, MASS-TO-CHARGE RATIO m/z, DETECTION INTENSITY I, ANALYSIS CONDITION)

PEPTIDE NAME /SEQUENCE	m [Da]	z [–]	m/z	I	τ [min]	ANALYSIS CONDITION (EXAMPLE: ORDER OF TANDEM ANALYSIS)
PEPTIDE A	200	1	200	15160	20	2
PEPTIDE B	700	2	350	2100	28	3
PEPTIDE C	450	1	450	4754	35	2
⋮	⋮	⋮	⋮	⋮	⋮	⋮

• CHARACTERISTICS DATA OF A PEPTIDE DERIVED FROM A PROTEIN THAT HAS ONCE BEEN IDENTIFIED OR THAT SHOULD BE ELIMINATED FROM THE OBJECTS FOR TANDEM ANALYSIS
(PROTEIN NUMBER, ID NUMBER, MASS NUMBER m, RETENTION TIME IN LC τ, VALENCE z, MASS-TO-CHARGE RATIO m/z, DETECTION INTENSITY I, ANALYSIS CONDITION)

PEPTIDE NAME /SEQUENCE	PROTEIN NAME	m [Da]	z [–]	m/z	I	τ [min]	ANALYSIS CONDITION (EXAMPLE: ORDER OF TANDEM ANALYSIS)
PEPTIDE A	PROTEIN A	570	1	570	25010	25	2
PEPTIDE B	PROTEIN A	652	1	652	3140	32	3
PEPTIDE C	PROTEIN A	652	2	326	58754	45	2
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮
PEPTIDE D	PROTEIN B	1042	2	521	6456	22	2
PEPTIDE E	PROTEIN B	718	2	359	3080	35	3
PEPTIDE F	PROTEIN B	671	2	335.5	8054	48	3
⋮	⋮	⋮	⋮	⋮	⋮	⋮	⋮

• CHARACTERISTICS DATA OF A SUGAR CHAIN THAT HAS ONCE BEEN SUBJECTED TO MS^n ($n \geq 2$) MEASUREMENT
(MASS NUMBER m, RETENTION TIME IN LC τ, VALENCE z, MASS-TO-CHARGE RATIO m/z, DETECTION INTENSITY I, ANALYSIS CONDITION)

SUGAR CHAIN NAME /STRUCTURE	m [Da]	z [–]	m/z	I	τ [min]	ANALYSIS CONDITION (EXAMPLE: ORDER OF TANDEM ANALYSIS)
SUGAR CHAIN A	1002	2	501	15710	55	2
SUGAR CHAIN B	840	2	420	8340	34	3
SUGAR CHAIN C	1280	2	640	10754	42	2
⋮	⋮	⋮	⋮	⋮	⋮	⋮

• CHARACTERISTICS DATA OF A CHEMICAL SUBSTANCE THAT HAS ONCE BEEN SUBJECTED TO MS^n ($n \geq 2$) MEASUREMENT
(MASS NUMBER m, RETENTION TIME IN LC τ, VALENCE z, MASS-TO-CHARGE RATIO m/z, DETECTION INTENSITY I, ANALYSIS CONDITION)

CHEMICAL SUBSTANCE NAME/STRUCTURE	m [Da]	z [–]	m/z	I	τ [min]	ANALYSIS CONDITION (EXAMPLE: ORDER OF TANDEM ANALYSIS)
CHEMICAL SUBSTANCE A	270	1	270	85510	23	2
CHEMICAL SUBSTANCE B	358	1	358	9840	47	2
CHEMICAL SUBSTANCE C	682	2	341	20764	82	2
⋮	⋮	⋮	⋮	⋮	⋮	⋮

•CHARACTERISTICS DATA OF AN ION SPECIES DERIVED FROM NOISE OR IMPURITIES
(MASS NUMBER m, RETENTION TIME IN LC τ, VALENCE z, MASS-TO-CHARGE RATIO m/z, DETECTION INTENSITY I, ANALYSIS CONDITION)

m [Da]	z [–]	m/z	I	τ [min]	ANALYSIS CONDITION (EXAMPLE: ORDER OF TANDEM ANALYSIS)
361	1	361	–	15	–
640	1	640	–	40	–
740	1	740	–	31	–
⋮	⋮	⋮	⋮	⋮	⋮

FIG. 6

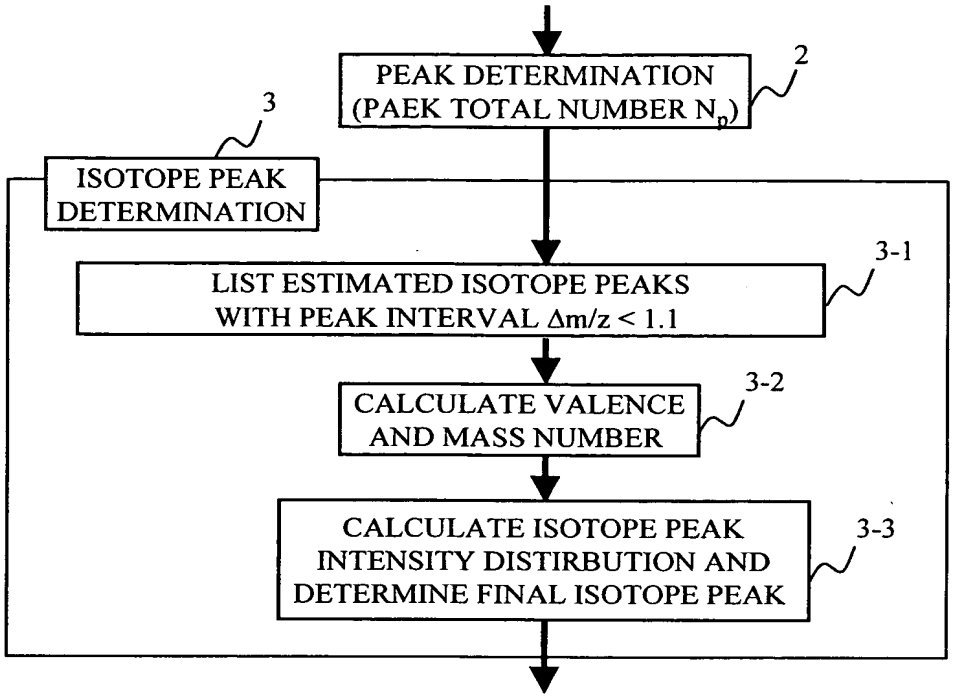

PEAK DETERMINATION
(PAEK TOTAL NUMBER N_p)
2
3
ISOTOPE PEAK
DETERMINATION
3-1
LIST ESTIMATED ISOTOPE PEAKS
WITH PEAK INTERVAL Δm/z < 1.1
3-2
CALCULATE VALENCE
AND MASS NUMBER
3-3
CALCULATE ISOTOPE PEAK
INTENSITY DISTIRBUTION AND
DETERMINE FINAL ISOTOPE PEAK

FIG. 7

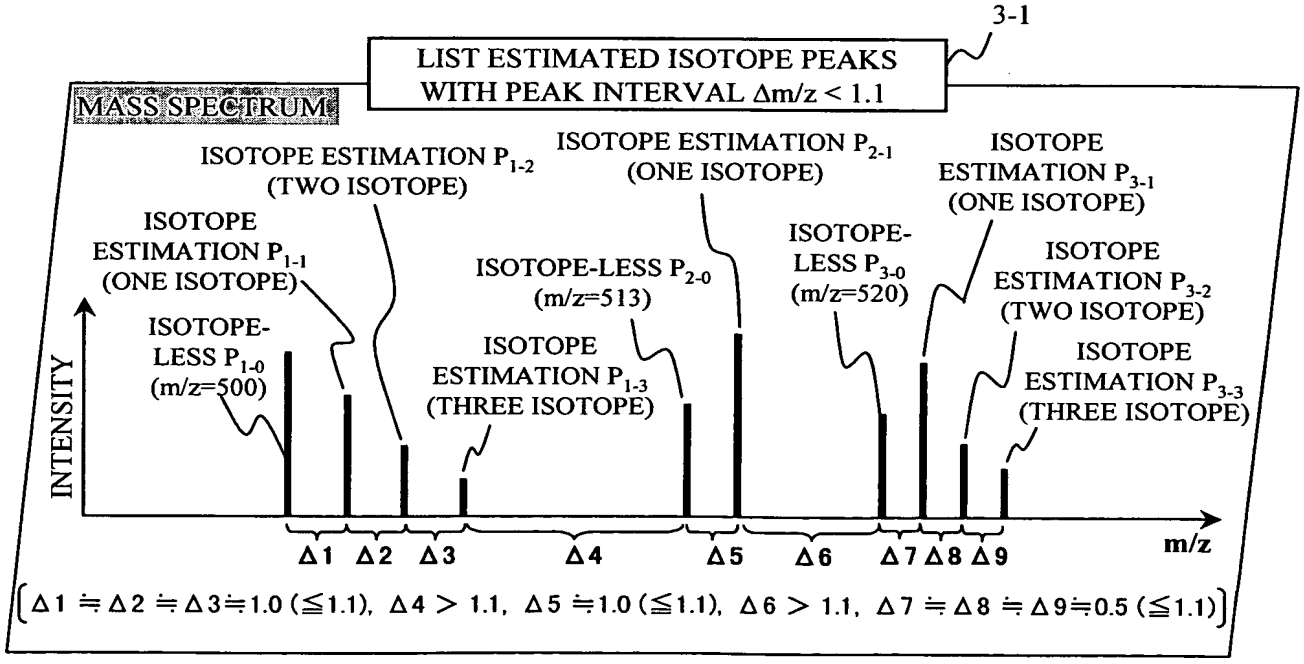

3-1
LIST ESTIMATED ISOTOPE PEAKS
WITH PEAK INTERVAL Δm/z < 1.1
MASS SPECTRUM
ISOTOPE ESTIMATION P_{1-2}
(TWO ISOTOPE)
ISOTOPE ESTIMATION P_{2-1}
(ONE ISOTOPE)
ISOTOPE
ESTIMATION P_{3-1}
(ONE ISOTOPE)
ISOTOPE
ESTIMATION P_{1-1}
(ONE ISOTOPE)
ISOTOPE-LESS P_{2-0}
(m/z=513)
ISOTOPE-
LESS P_{3-0}
(m/z=520)
ISOTOPE
ESTIMATION P_{3-2}
(TWO ISOTOPE)
ISOTOPE-
LESS P_{1-0}
(m/z=500)
ISOTOPE
ESTIMATION P_{1-3}
(THREE ISOTOPE)
ISOTOPE
ESTIMATION P_{3-3}
(THREE ISOTOPE)
INTENSITY
Δ1 Δ2 Δ3 Δ4 Δ5 Δ6 Δ7 Δ8 Δ9
m/z
(Δ1 ≒ Δ2 ≒ Δ3 ≒ 1.0 (≦1.1), Δ4 > 1.1, Δ5 ≒ 1.0 (≦1.1), Δ6 > 1.1, Δ7 ≒ Δ8 ≒ Δ9 ≒ 0.5 (≦1.1))

FIG. 8

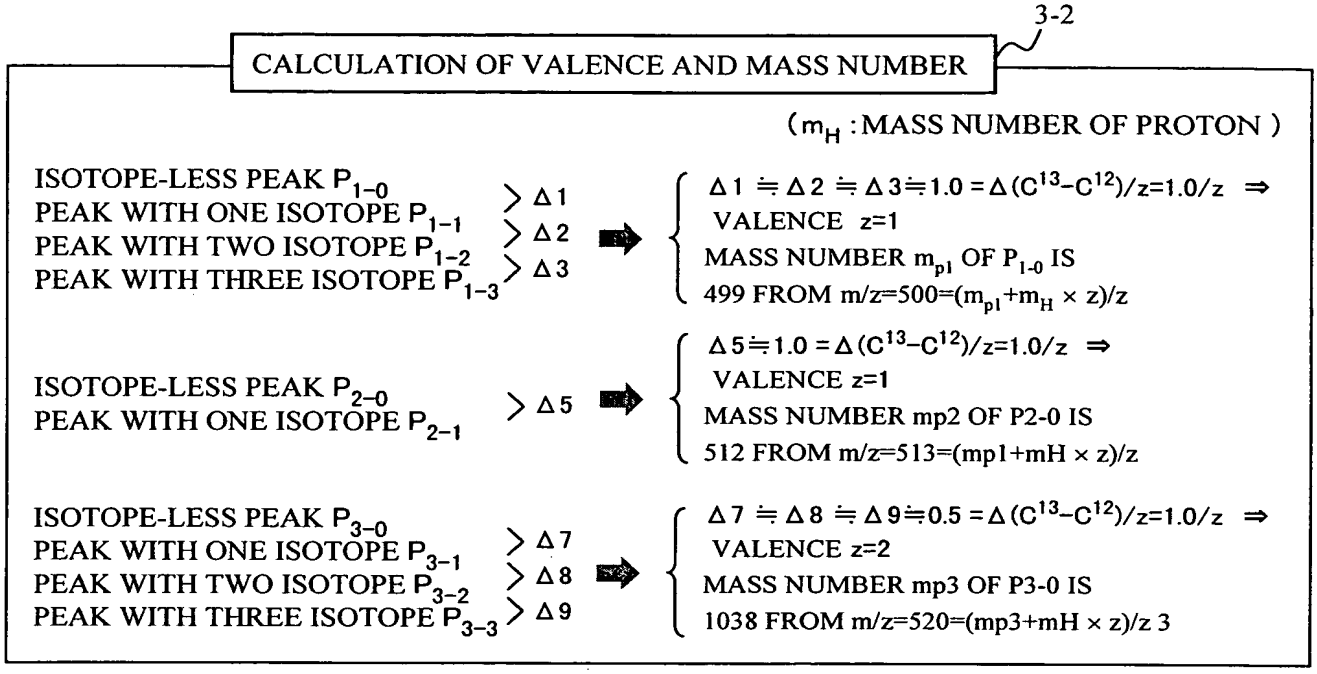

3-2
CALCULATION OF VALENCE AND MASS NUMBER
(m_H : MASS NUMBER OF PROTON)
ISOTOPE-LESS PEAK P_{1-0}
PEAK WITH ONE ISOTOPE P_{1-1}
PEAK WITH TWO ISOTOPE P_{1-2}
PEAK WITH THREE ISOTOPE P_{1-3}
> Δ1
> Δ2
> Δ3
Δ1 ≒ Δ2 ≒ Δ3 ≒ 1.0 = Δ(C^{13}–C^{12})/z=1.0/z ⇒
VALENCE z=1
MASS NUMBER m_{p1} OF P_{1-0} IS
499 FROM m/z=500=(m_{p1}+m_H × z)/z
ISOTOPE-LESS PEAK P_{2-0}
PEAK WITH ONE ISOTOPE P_{2-1}
> Δ5
Δ5 ≒ 1.0 = Δ(C^{13}–C^{12})/z=1.0/z ⇒
VALENCE z=1
MASS NUMBER mp2 OF P2-0 IS
512 FROM m/z=513=(mp1+mH × z)/z
ISOTOPE-LESS PEAK P_{3-0}
PEAK WITH ONE ISOTOPE P_{3-1}
PEAK WITH TWO ISOTOPE P_{3-2}
PEAK WITH THREE ISOTOPE P_{3-3}
> Δ7
> Δ8
> Δ9
Δ7 ≒ Δ8 ≒ Δ9 ≒ 0.5 = Δ(C^{13}–C^{12})/z=1.0/z ⇒
VALENCE z=2
MASS NUMBER mp3 OF P3-0 IS
1038 FROM m/z=520=(mp3+mH × z)/z 3

FIG. 9 A

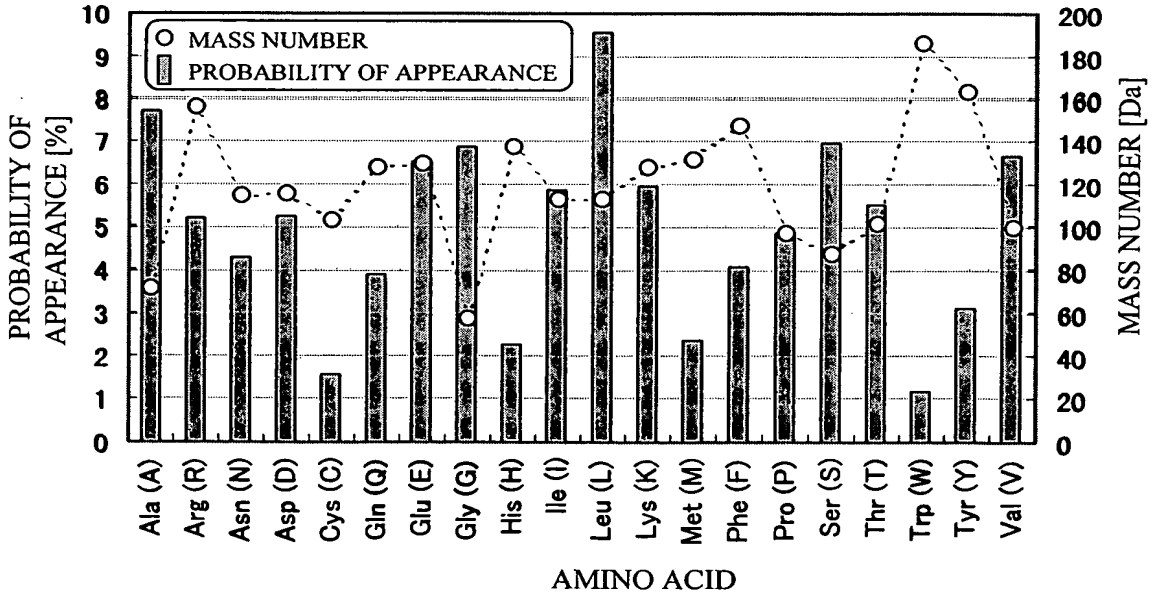

MASS NUMBER
PROBABILITY OF APPEARANCE
PROBABILITY OF APPEARANCE [%]
MASS NUMBER [Da]
0
1
2
3
4
5
6
7
8
9
10
0
20
40
60
80
100
120
140
160
180
200
Ala (A)
Arg (R)
Asn (N)
Asp (D)
Cys (C)
Gln (Q)
Glu (E)
Gly (G)
His (H)
Ile (I)
Leu (L)
Lys (K)
Met (M)
Phe (F)
Pro (P)
Ser (S)
Thr (T)
Trp (W)
Tyr (Y)
Val (V)
AMINO ACID

FIG. 9 B

3-3

CALCULATION OF ISOTOPE PEAK INTENSITY DISTRIBUTION AND DETERMINATION OF FINAL ISOTOPE PEAK

CALCULATION OF EACH ELEMENT NUMBER FROM MASS NUMBER

IN THE CASE OF A PEPTIDE ($C_{Nc}N_{Nn}H_{Nh}O_{No}S_{Ns}$)

NUMBER OF C: Nc= m ×nC / 111.1807
NUMBER OF O: No= m ×nO / 111.1807
NUMBER OF N: Nn= m ×nN / 111.1807
NUMBER OF H: Nh= m ×nH / 111.1807
NUMBER OF S : Ns= m ×nS / 111.1807

TABLE A: EACH ELEMENT NUMBER PER AVEARAGE AMINO ACID

nC	nO	nN	nH	nS
4.9583	1.4733	1.3547	7.8185	0.0396

CALCULATION OF ISOTOPE PEAK INTENSITY DISTRIBUTION

IN THE CASE WHERE ONLY AN ISOTOPE (C^{13}) IS CONSIDERED

ISOTOPE PEAK INTENSITY P_{Nix}
(WHEN NUMBER OF ISOTOPES IS Nis):

$$P_{Nis} = [{}_{Nc}C_{Nis} \cdot pC(1)^{(Nc-Nis)} \cdot pC(2)^{Nis}] \times pH(1)^{Nh} \cdot pN(1)^{Nn} \cdot pO(1)^{No} \cdot pS(1)^{Ns}$$

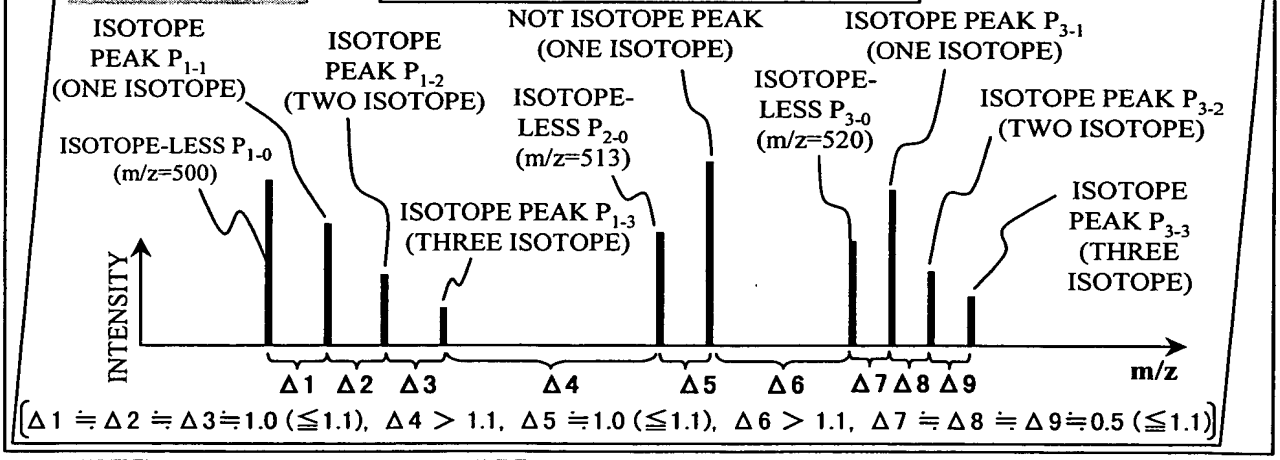
TABLE B: MASS NUMBER AND ABUNDANCE RATIO OF EACH ISOTOPE ELEMENT

	MASS NUMBER		ABUNDANCE RATIO	
C	mC(1)	12	pC(1)	0.9889
	mC(2)	13.003354	pC(2)	0.0111
H	mH(1)	1.007825	pH(1)	0.9999
	mH(2)	2.014102	pH(2)	0.0001
N	mN(1)	14.003074	pN(1)	0.9963
	mN(2)	15.000108	pN(2)	0.0037
O	mO(1)	15.994915	pO(1)	0.9976
	mO(2)	16.999133	pO(2)	0.0004
	mO(3)	17.999160	pO(3)	0.0020
S	mS(1)	31.972074	pS(1)	0.9502
	mS(2)	32.971460	pS(2)	0.0075
	mS(3)	33.967864	pS(3)	0.0422
	mS(4)	35.967091	pS(4)	0.0001

DETERMINATION OF FINAL ISOTOPE PEAK

OF THE ESTIMATED ISOTOPE PEAKS, AN INTENSITY DISTRIBUTION CALUCATED VALUE P_{Nis} OF ISOTOPE PEAKS AGREES WITH A RELATIVE VALUE OF A RELATIVE MEASURED INTENSITY FORISOTOPE-LESS PEAKS WITH AN ERROR OF LESS THAN 50%

FINALLY DETERMINE THE ESTIMATED ISOTOPE PEAK AS AN ISOTOPE PEAK



$[\Delta 1 \fallingdotseq \Delta 2 \fallingdotseq \Delta 3 \fallingdotseq 1.0\ (\leqq 1.1),\ \Delta 4 > 1.1,\ \Delta 5 \fallingdotseq 1.0\ (\leqq 1.1),\ \Delta 6 > 1.1,\ \Delta 7 \fallingdotseq \Delta 8 \fallingdotseq \Delta 9 \fallingdotseq 0.5\ (\leqq 1.1)]$

FIG. 10

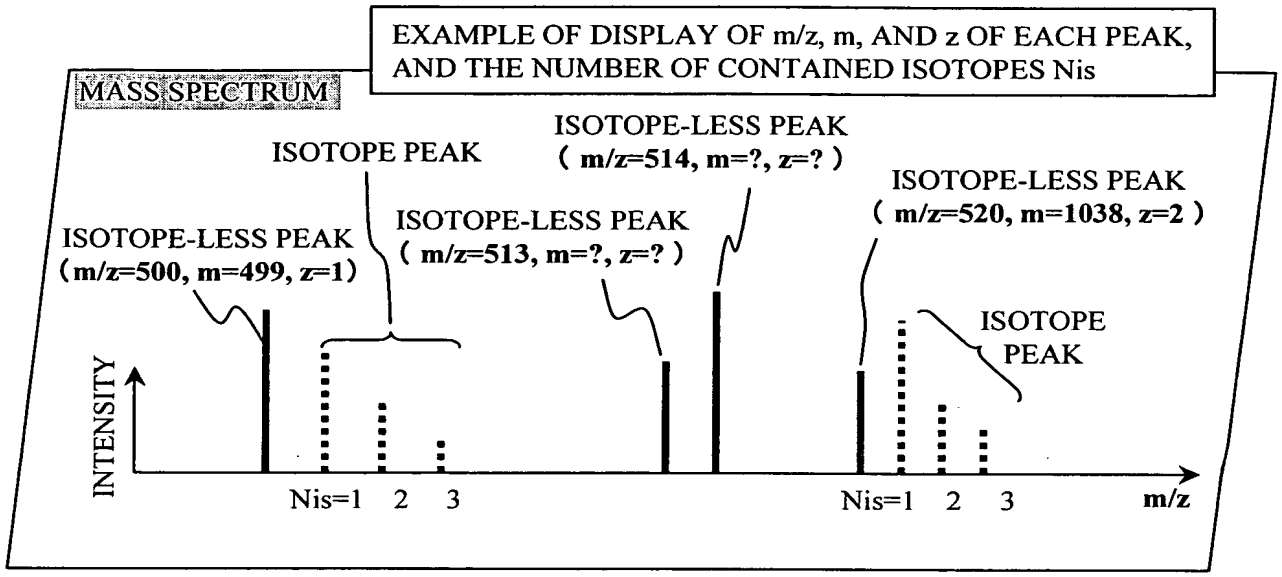

EXAMPLE OF DISPLAY OF m/z, m, AND z OF EACH PEAK, AND THE NUMBER OF CONTAINED ISOTOPES Nis
MASS SPECTRUM
ISOTOPE PEAK
ISOTOPE-LESS PEAK (m/z=514, m=?, z=?)
ISOTOPE-LESS PEAK (m/z=520, m=1038, z=2)
ISOTOPE-LESS PEAK (m/z=500, m=499, z=1)
ISOTOPE-LESS PEAK (m/z=513, m=?, z=?)
ISOTOPE PEAK
INTENSITY
Nis=1 2 3
Nis=1 2 3
m/z

FIG. 11

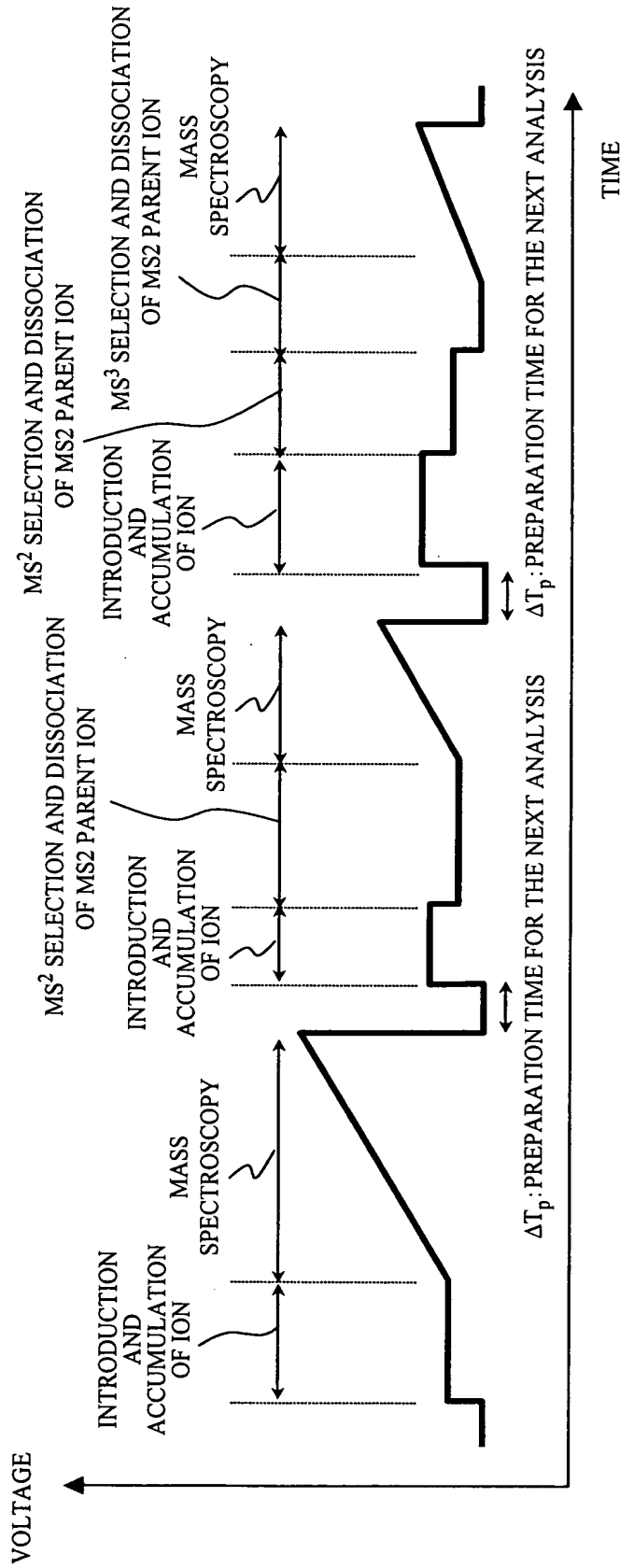

VOLTAGE
TIME
MS¹ANALYSIS
MS²ANALYSIS
MS³ANALYSIS
INTRODUCTION AND ACCUMULATION OF ION
MASS SPECTROSCOPY
MS² SELECTION AND DISSOCIATION OF MS2 PARENT ION
MS³ SELECTION AND DISSOCIATION OF MS2 PARENT ION
ΔTp: PREPARATION TIME FOR THE NEXT ANALYSIS

FIG. 12

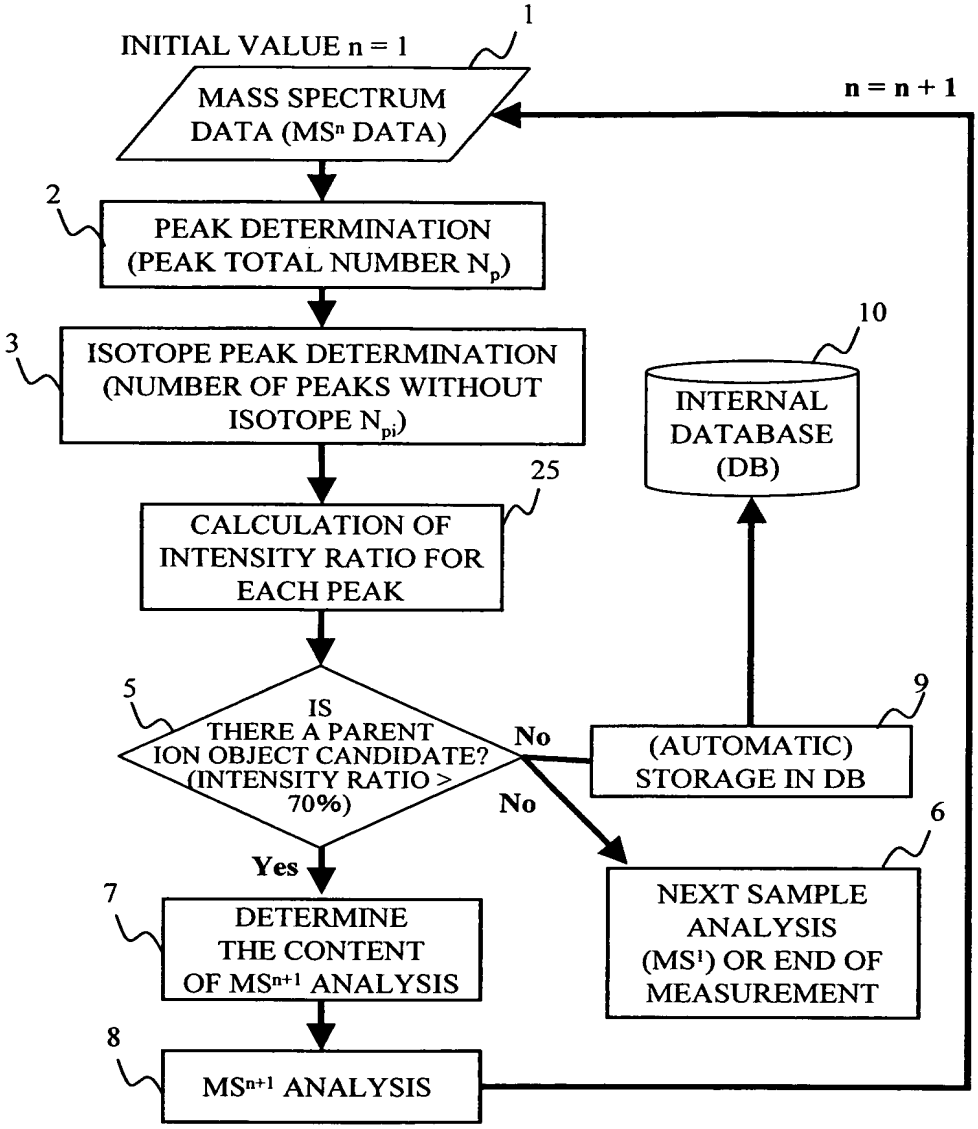

1
INITIAL VALUE n = 1
MASS SPECTRUM DATA (MSⁿ DATA)
n = n + 1
2
PEAK DETERMINATION (PEAK TOTAL NUMBER N_p)
3
ISOTOPE PEAK DETERMINATION (NUMBER OF PEAKS WITHOUT ISOTOPE N_{pi})
10
INTERNAL DATABASE (DB)
25
CALCULATION OF INTENSITY RATIO FOR EACH PEAK
5
IS THERE A PARENT ION OBJECT CANDIDATE? (INTENSITY RATIO > 70%)
No
9
(AUTOMATIC) STORAGE IN DB
No
6
NEXT SAMPLE ANALYSIS (MS¹) OR END OF MEASUREMENT
Yes
7
DETERMINE THE CONTENT OF MSⁿ⁺¹ ANALYSIS
8
MSⁿ⁺¹ ANALYSIS

FIG. 13

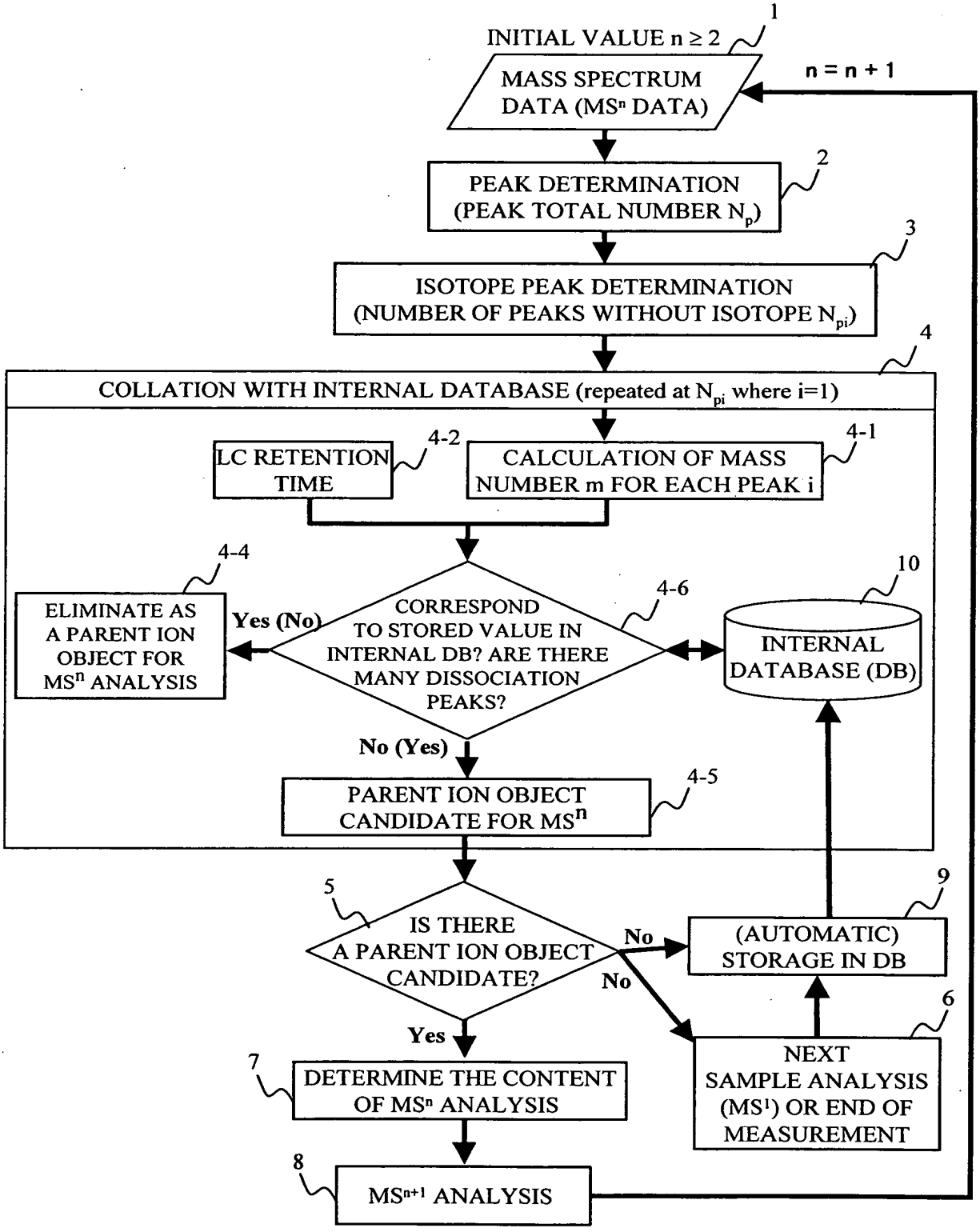

1
INITIAL VALUE n ≥ 2
MASS SPECTRUM DATA (MSⁿ DATA)
n = n + 1
2
PEAK DETERMINATION (PEAK TOTAL NUMBER Np)
3
ISOTOPE PEAK DETERMINATION (NUMBER OF PEAKS WITHOUT ISOTOPE Npi)
4
COLLATION WITH INTERNAL DATABASE (repeated at Npi where i=1)
4-2
LC RETENTION TIME
4-1
CALCULATION OF MASS NUMBER m FOR EACH PEAK i
4-4
ELIMINATE AS A PARENT ION OBJECT FOR MSⁿ ANALYSIS
Yes (No)
4-6
CORRESPOND TO STORED VALUE IN INTERNAL DB? ARE THERE MANY DISSOCIATION PEAKS?
10
INTERNAL DATABASE (DB)
No (Yes)
4-5
PARENT ION OBJECT CANDIDATE FOR MSⁿ
5
IS THERE A PARENT ION OBJECT CANDIDATE?
No
9
(AUTOMATIC) STORAGE IN DB
No
6
NEXT SAMPLE ANALYSIS (MS1) OR END OF MEASUREMENT
Yes
7
DETERMINE THE CONTENT OF MSⁿ ANALYSIS
8
MSⁿ⁺¹ ANALYSIS

FIG. 14

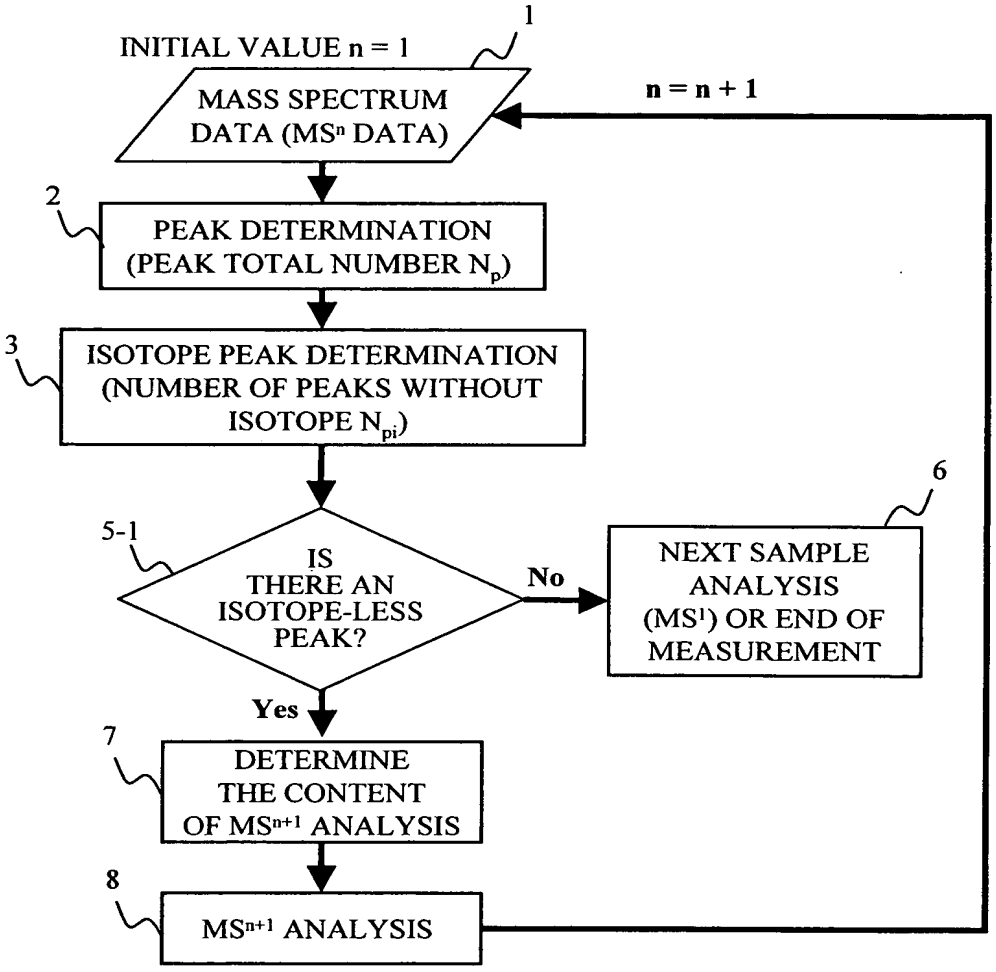

1
INITIAL VALUE n = 1
MASS SPECTRUM DATA (MSⁿ DATA)
n = n + 1
2
PEAK DETERMINATION (PEAK TOTAL NUMBER N_p)
3
ISOTOPE PEAK DETERMINATION (NUMBER OF PEAKS WITHOUT ISOTOPE N_{pi})
5-1
IS THERE AN ISOTOPE-LESS PEAK?
No
6
NEXT SAMPLE ANALYSIS (MS¹) OR END OF MEASUREMENT
Yes
7
DETERMINE THE CONTENT OF MSⁿ⁺¹ ANALYSIS
8
MSⁿ⁺¹ ANALYSIS

FIG. 15

ISOTOPE PEAK INTENSITY DISTRIBUTION
PATTERNS DEPENDING ON ION MASS NUMBER

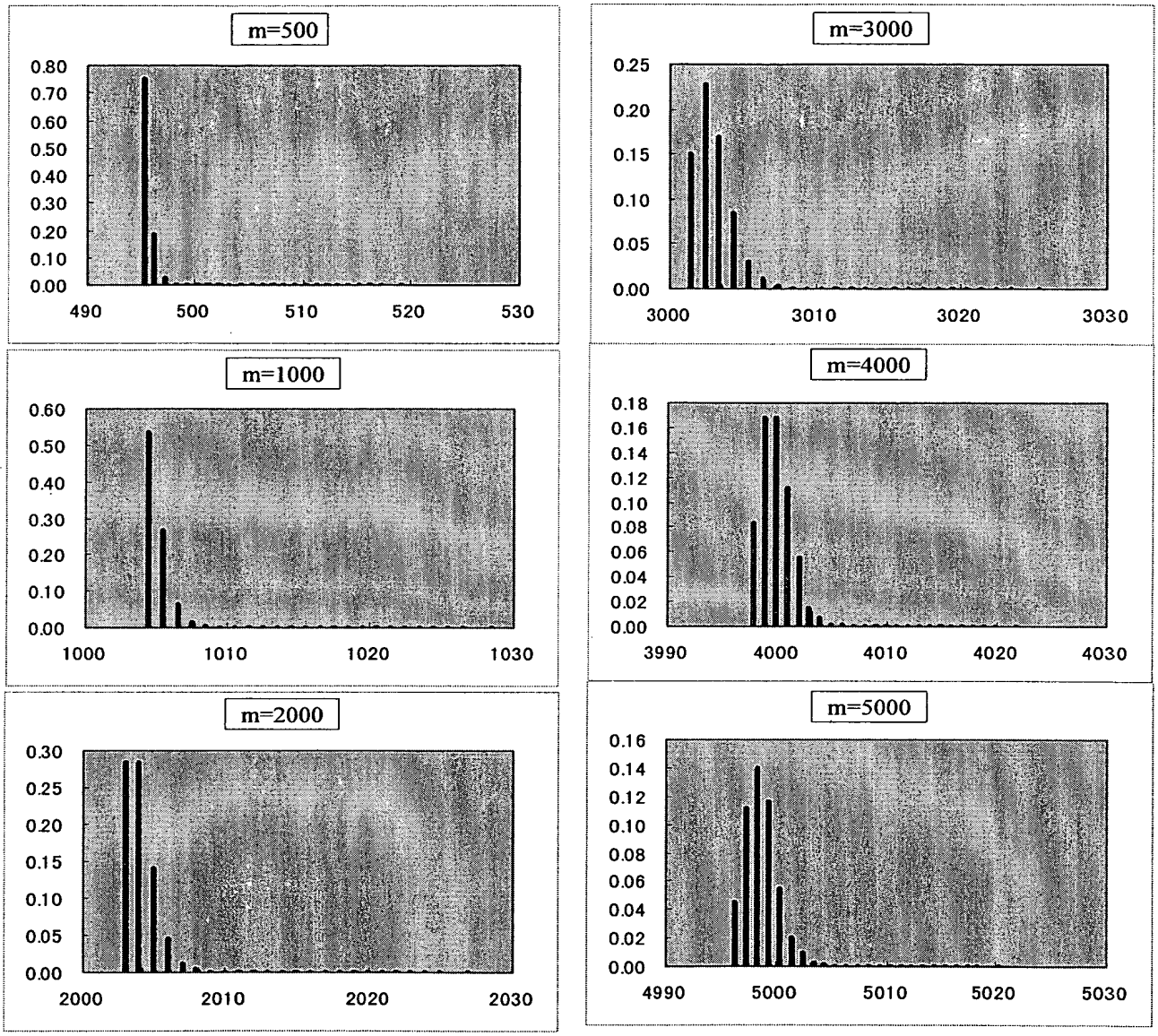


FIG. 16

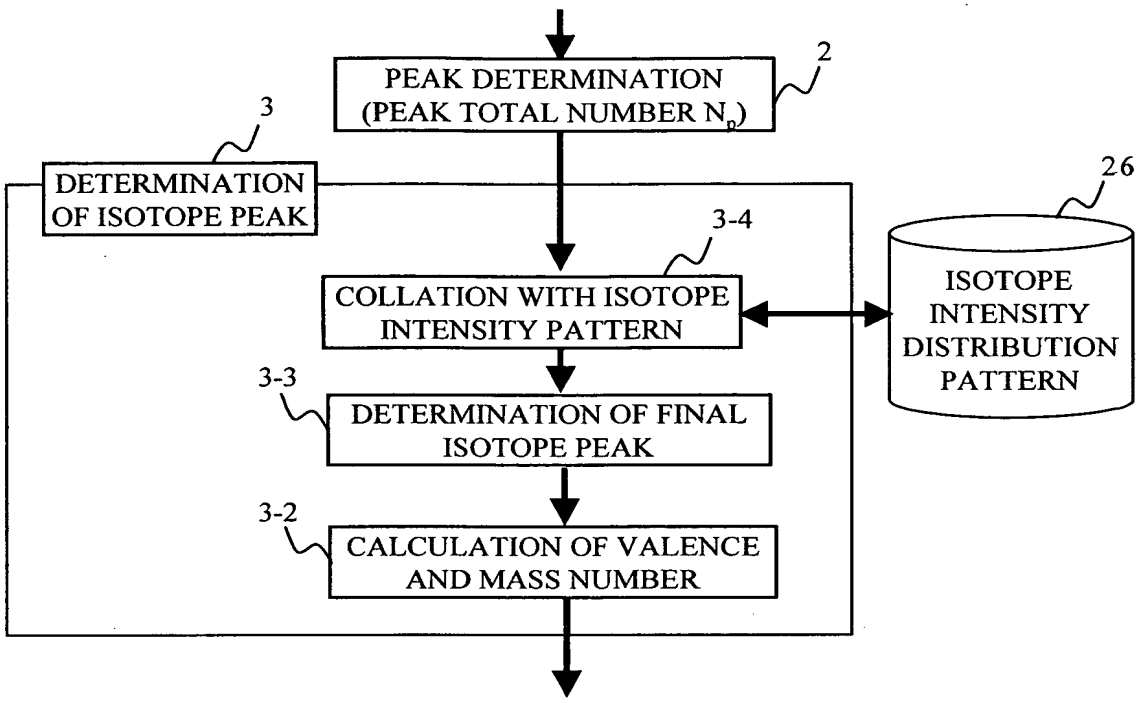

PEAK DETERMINATION
(PEAK TOTAL NUMBER N_p)
2
3
DETERMINATION OF ISOTOPE PEAK
26
3-4
COLLATION WITH ISOTOPE INTENSITY PATTERN
ISOTOPE INTENSITY DISTRIBUTION PATTERN
3-3
DETERMINATION OF FINAL ISOTOPE PEAK
3-2
CALCULATION OF VALENCE AND MASS NUMBER

FIG. 17

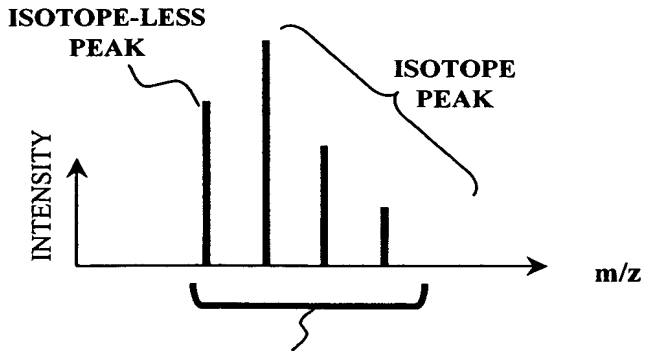

ISOTOPE-LESS PEAK
ISOTOPE PEAK
INTENSITY
m/z
SELECT AN ION CONTAINING ISOTOPE PEAKS AS THE NEXT ANALYSIS TARGET ION

FIG. 18

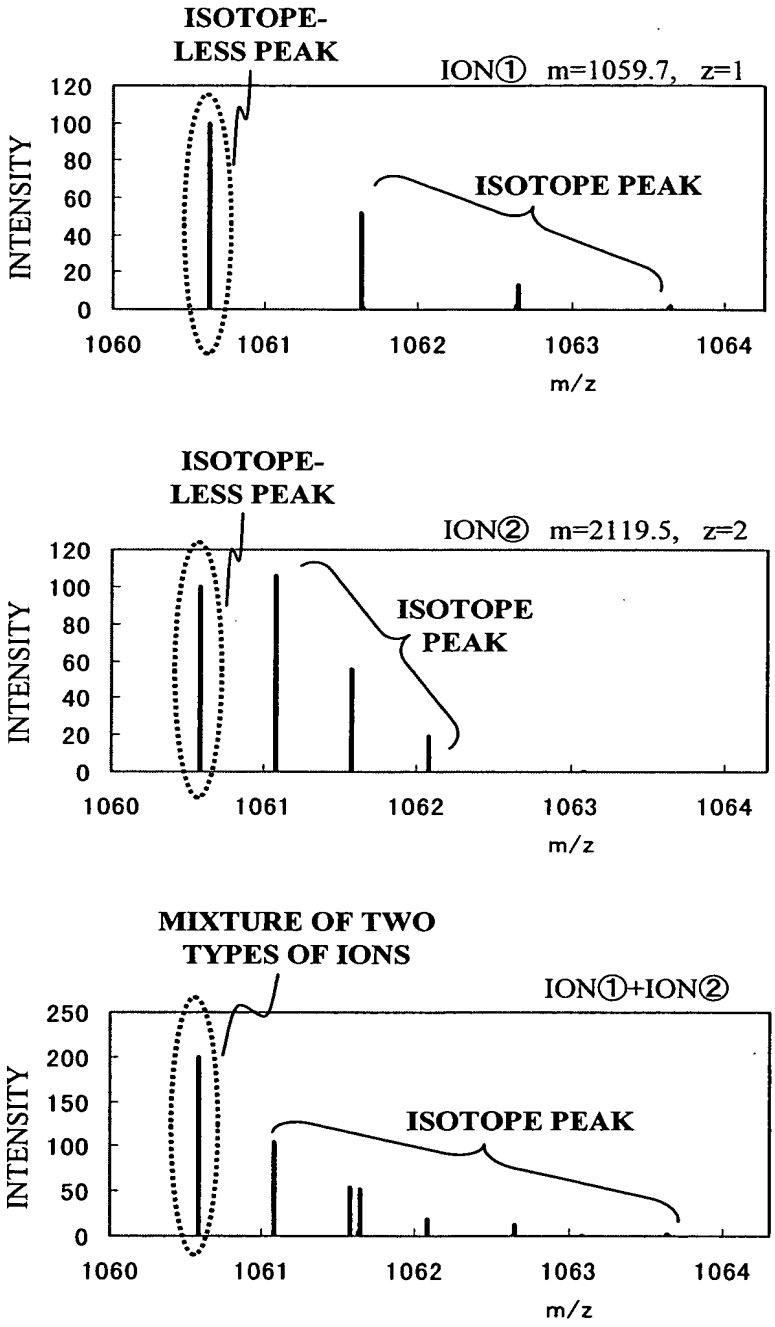

ISOTOPE-
LESS PEAK
ION① m=1059.7, z=1
ISOTOPE PEAK
INTENSITY
120
100
80
60
40
20
0
1060
1061
1062
1063
1064
m/z
ISOTOPE-
LESS PEAK
ION② m=2119.5, z=2
ISOTOPE
PEAK
INTENSITY
120
100
80
60
40
20
0
1060
1061
1062
1063
1064
m/z
MIXTURE OF TWO
TYPES OF IONS
ION①+ION②
ISOTOPE PEAK
INTENSITY
250
200
150
100
50
0
1060
1061
1062
1063
1064
m/z

FIG. 19

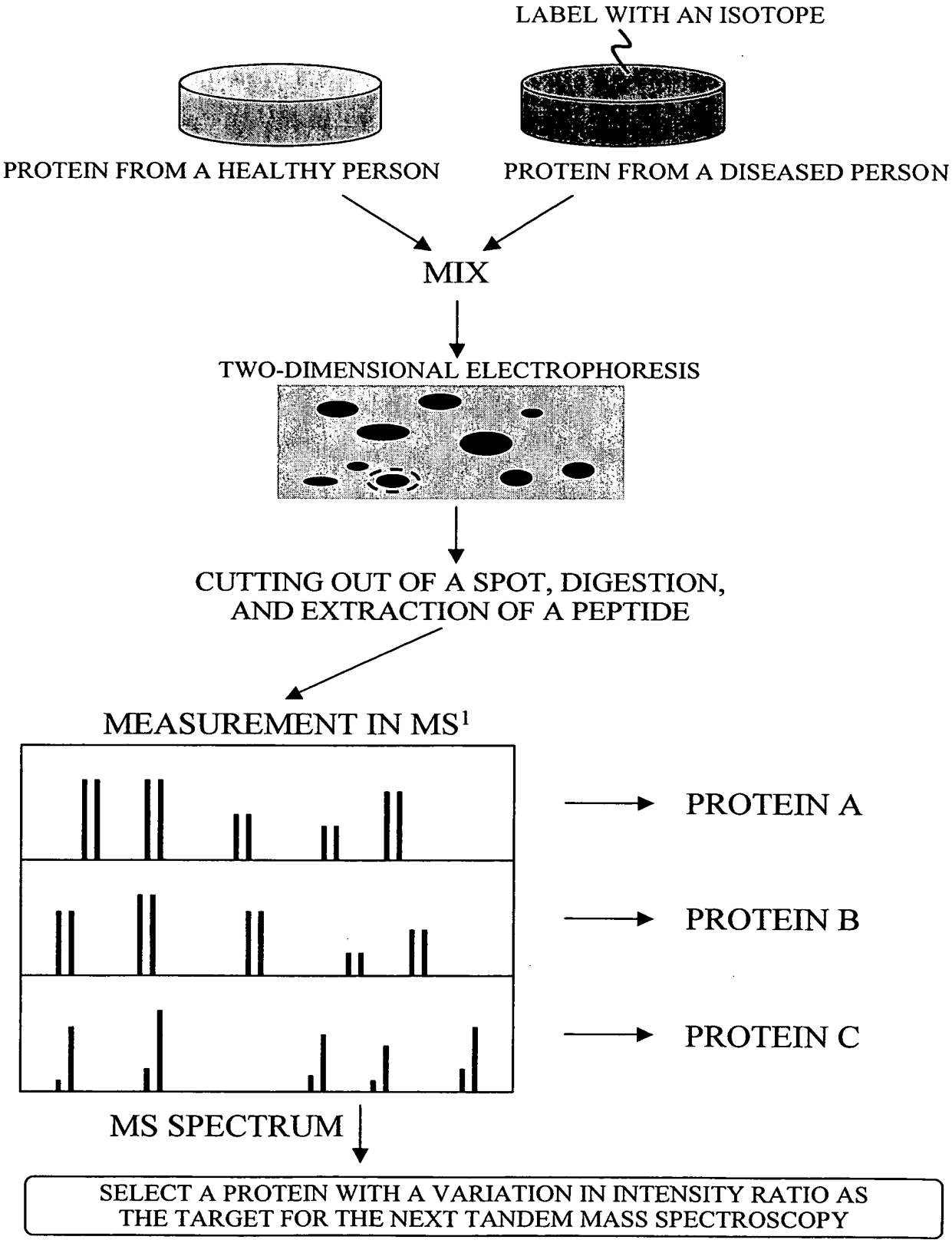

LABEL WITH AN ISOTOPE
PROTEIN FROM A HEALTHY PERSON
PROTEIN FROM A DISEASED PERSON
MIX
TWO-DIMENSIONAL ELECTROPHORESIS
CUTTING OUT OF A SPOT, DIGESTION, AND EXTRACTION OF A PEPTIDE
MEASUREMENT IN MS1
PROTEIN A
PROTEIN B
PROTEIN C
MS SPECTRUM
SELECT A PROTEIN WITH A VARIATION IN INTENSITY RATIO AS THE TARGET FOR THE NEXT TANDEM MASS SPECTROSCOPY

FIG. 20

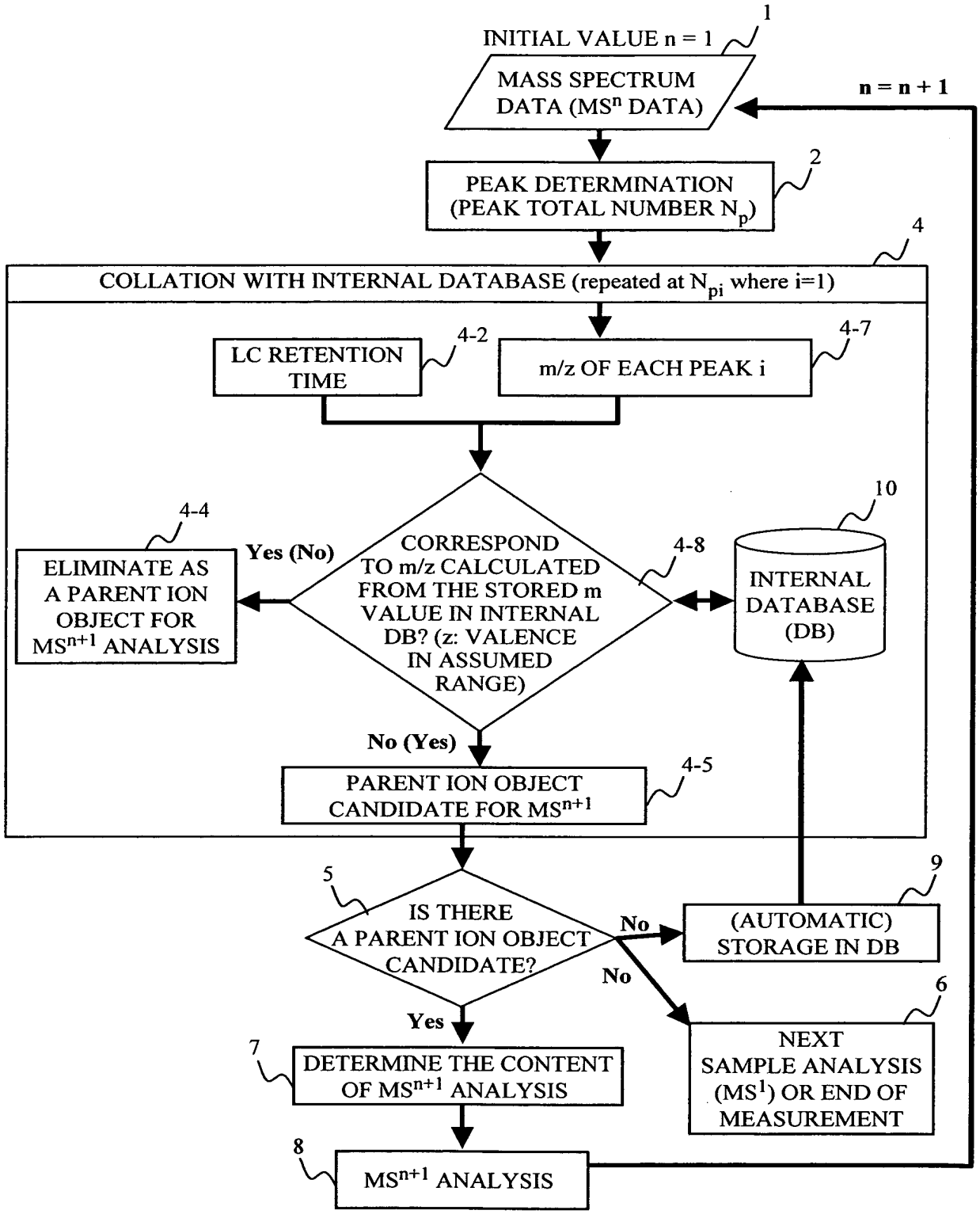

1
INITIAL VALUE n = 1
MASS SPECTRUM DATA (MS^n DATA)
n = n + 1
2
PEAK DETERMINATION (PEAK TOTAL NUMBER N_p)
4
COLLATION WITH INTERNAL DATABASE (repeated at N_pi where i=1)
4-2
LC RETENTION TIME
4-7
m/z OF EACH PEAK i
10
4-4
ELIMINATE AS A PARENT ION OBJECT FOR MS^n+1 ANALYSIS
Yes (No)
CORRESPOND TO m/z CALCULATED FROM THE STORED m VALUE IN INTERNAL DB? (z: VALENCE IN ASSUMED RANGE)
4-8
INTERNAL DATABASE (DB)
No (Yes)
4-5
PARENT ION OBJECT CANDIDATE FOR MS^n+1
5
IS THERE A PARENT ION OBJECT CANDIDATE?
No
9
(AUTOMATIC) STORAGE IN DB
No
6
Yes
7
DETERMINE THE CONTENT OF MS^n+1 ANALYSIS
NEXT SAMPLE ANALYSIS (MS^1) OR END OF MEASUREMENT
8
MS^n+1 ANALYSIS

FIG. 21

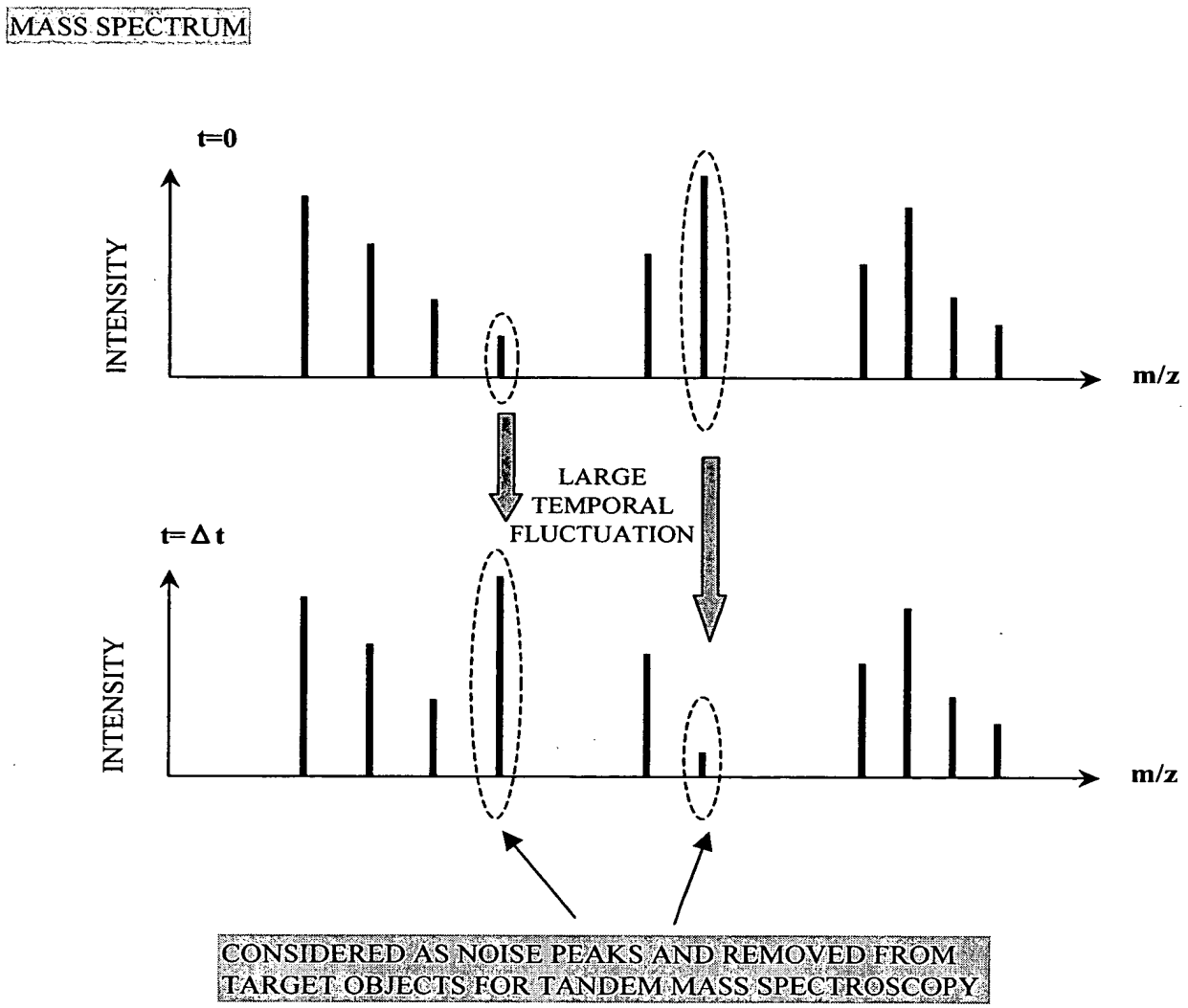

MASS SPECTRUM
t=0
INTENSITY
m/z
LARGE
TEMPORAL
FLUCTUATION
t=Δt
INTENSITY
m/z
CONSIDERED AS NOISE PEAKS AND REMOVED FROM
TARGET OBJECTS FOR TANDEM MASS SPECTROSCOPY

FIG. 22 a

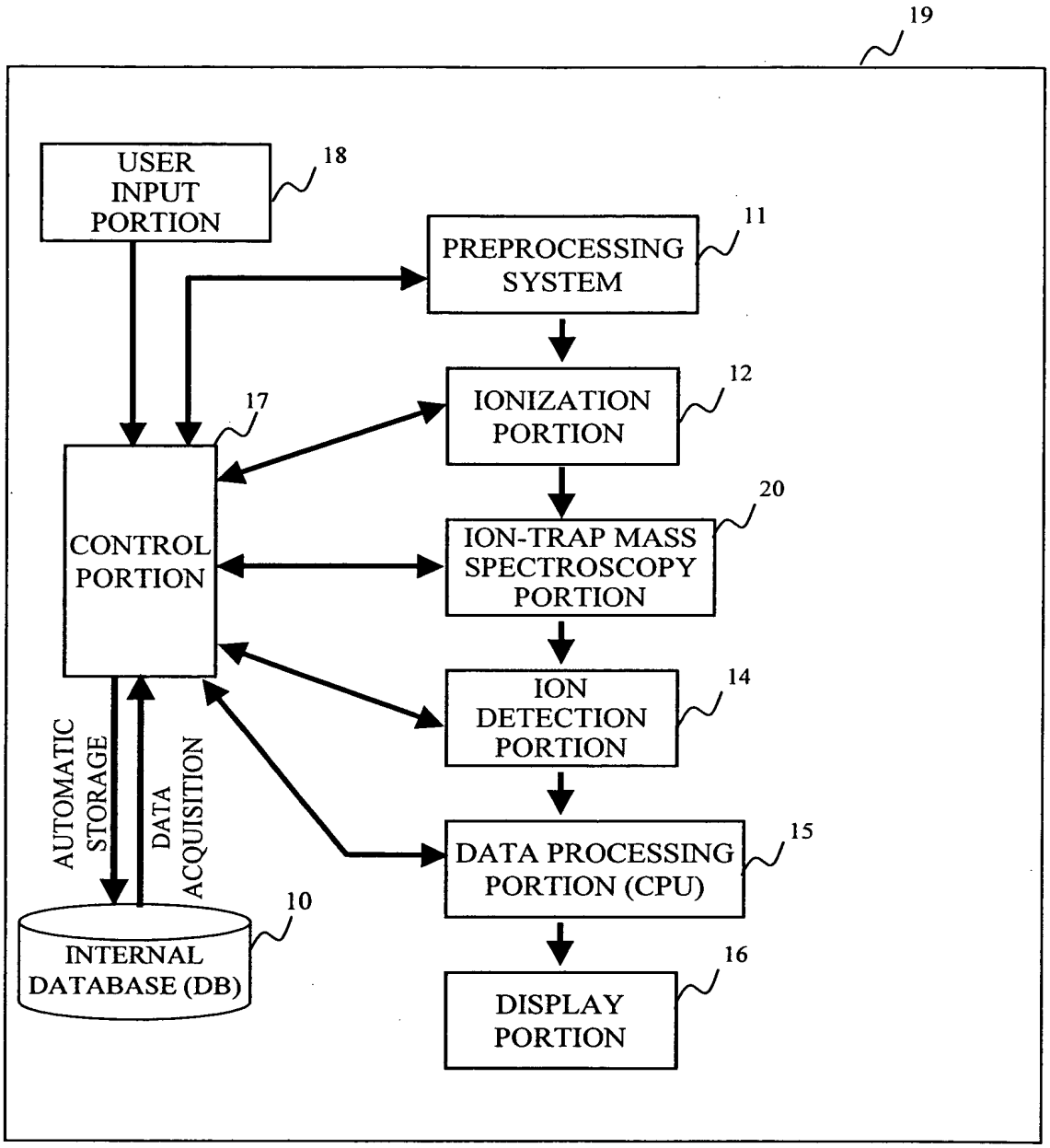

19
USER INPUT PORTION
18
PREPROCESSING SYSTEM
11
IONIZATION PORTION
12
17
CONTROL PORTION
20
ION-TRAP MASS SPECTROSCOPY PORTION
ION DETECTION PORTION
14
AUTOMATIC STORAGE
DATA ACQUISITION
DATA PROCESSING PORTION (CPU)
15
INTERNAL DATABASE (DB)
10
DISPLAY PORTION
16

FIG. 22 b

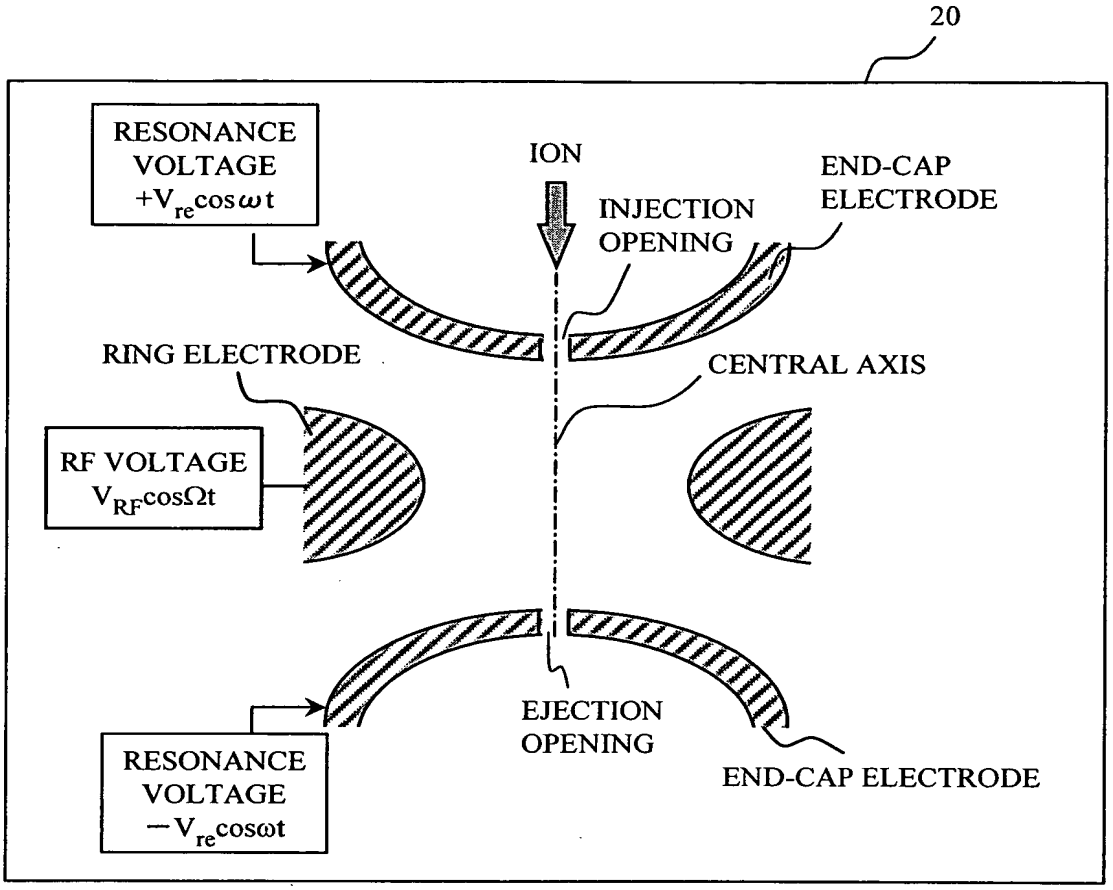

20
RESONANCE VOLTAGE $+V_{re}\cos\omega t$
ION
INJECTION OPENING
END-CAP ELECTRODE
RING ELECTRODE
CENTRAL AXIS
RF VOLTAGE $V_{RF}\cos\Omega t$
EJECTION OPENING
RESONANCE VOLTAGE $-V_{re}\cos\omega t$
END-CAP ELECTRODE

FIG. 23

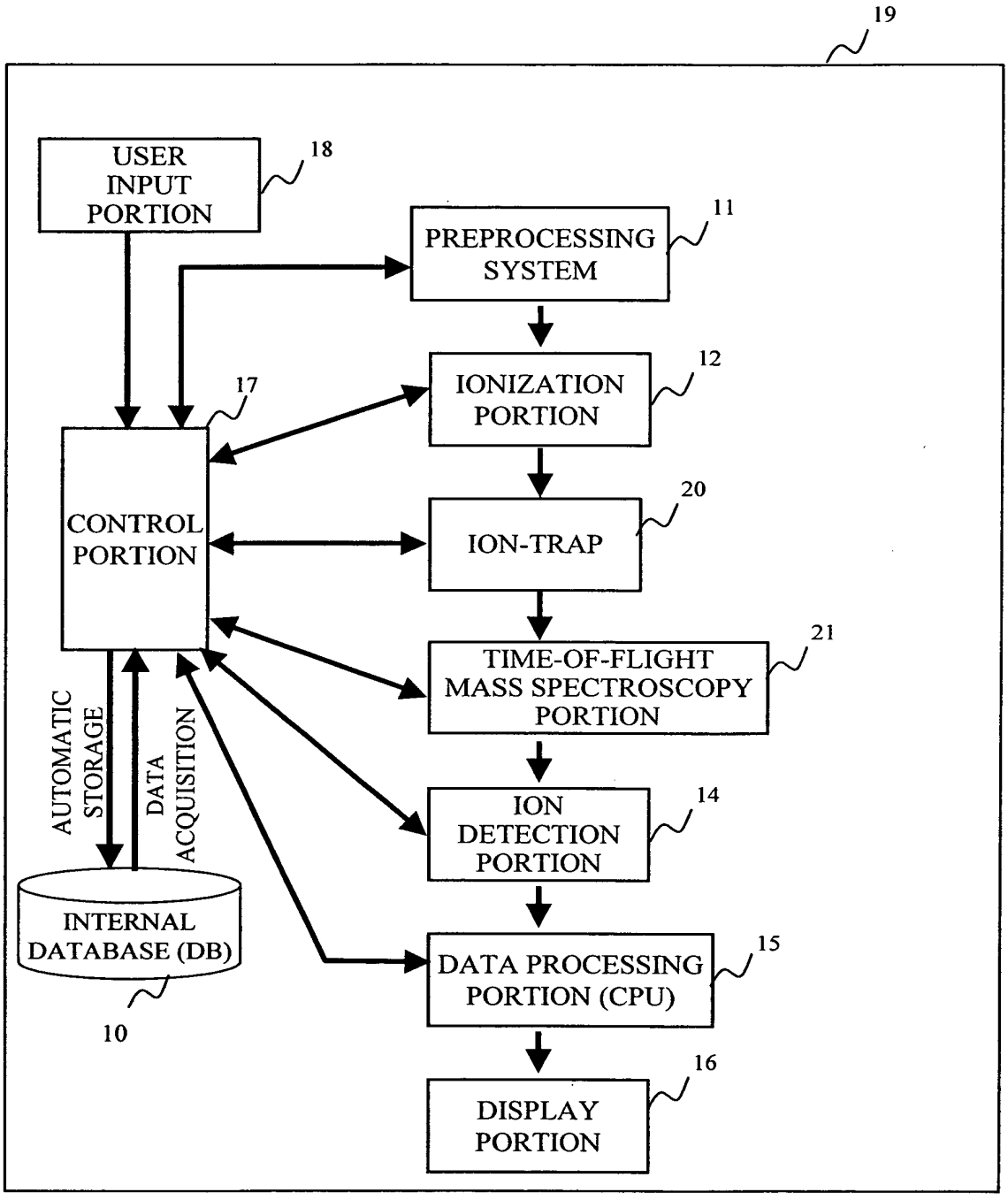

19
USER INPUT PORTION
18
PREPROCESSING SYSTEM
11
IONIZATION PORTION
12
17
CONTROL PORTION
ION-TRAP
20
TIME-OF-FLIGHT MASS SPECTROSCOPY PORTION
21
AUTOMATIC STORAGE
DATA ACQUISITION
ION DETECTION PORTION
14
INTERNAL DATABASE (DB)
10
DATA PROCESSING PORTION (CPU)
15
DISPLAY PORTION
16

FIG. 24 a

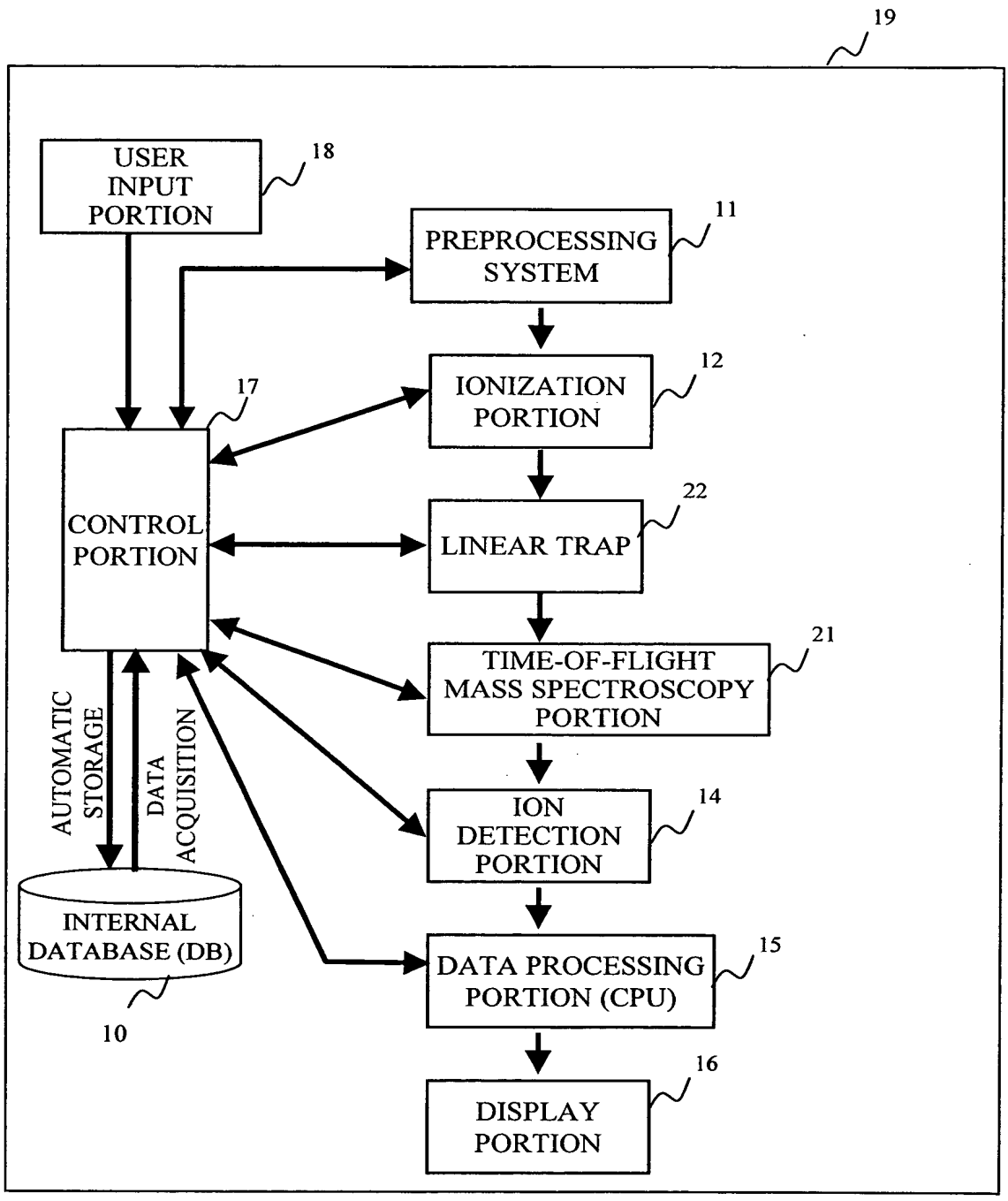

19
USER INPUT PORTION
18
PREPROCESSING SYSTEM
11
IONIZATION PORTION
12
17
CONTROL PORTION
LINEAR TRAP
22
TIME-OF-FLIGHT MASS SPECTROSCOPY PORTION
21
AUTOMATIC STORAGE
DATA ACQUISITION
ION DETECTION PORTION
14
INTERNAL DATABASE (DB)
10
DATA PROCESSING PORTION (CPU)
15
DISPLAY PORTION
16

FIG. 24 b

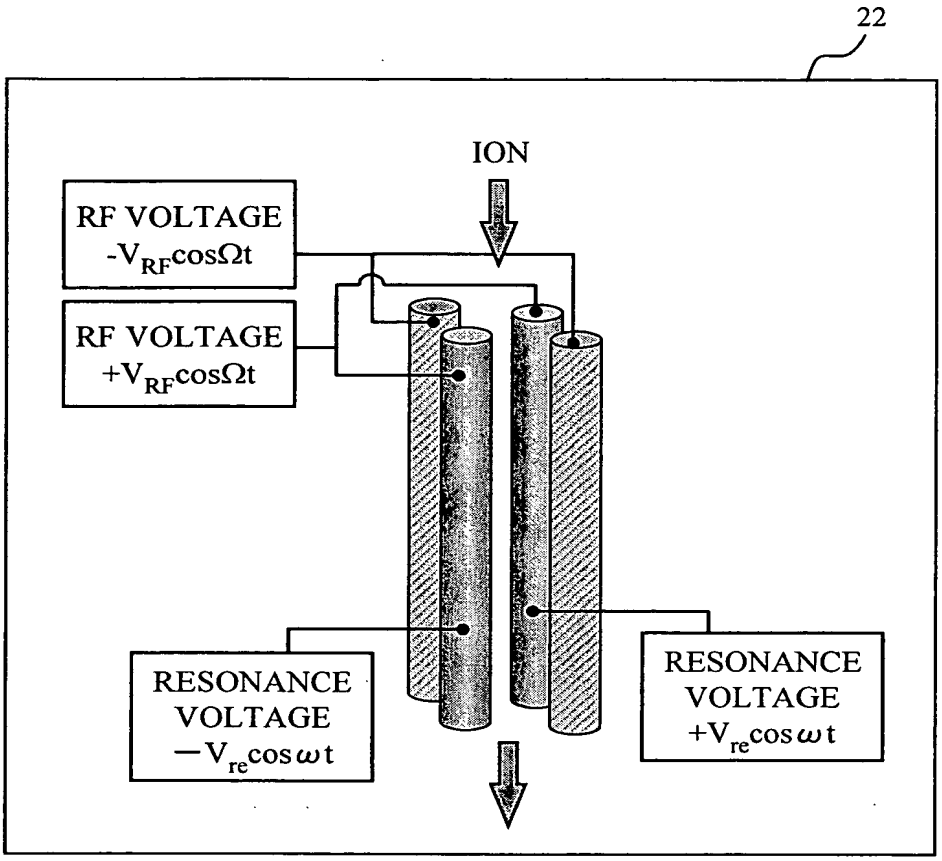

22
ION
RF VOLTAGE
$-V_{RF}\cos\Omega t$
RF VOLTAGE
$+V_{RF}\cos\Omega t$
RESONANCE
VOLTAGE
$-V_{re}\cos\omega t$
RESONANCE
VOLTAGE
$+V_{re}\cos\omega t$

FIG. 25

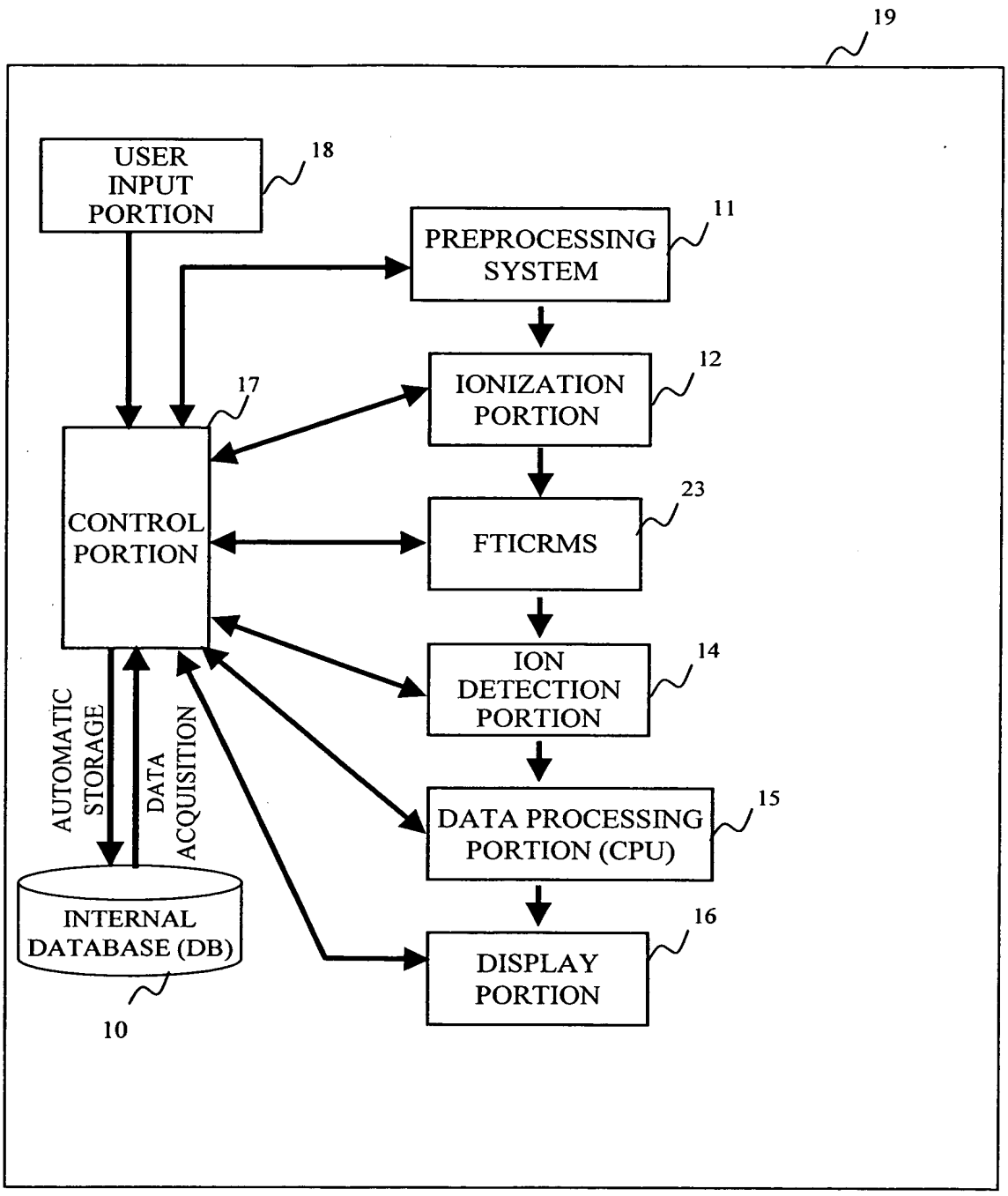

19
USER INPUT PORTION
18
PREPROCESSING SYSTEM
11
IONIZATION PORTION
12
17
CONTROL PORTION
23
FTICRMS
ION DETECTION PORTION
14
AUTOMATIC STORAGE
DATA ACQUISITION
DATA PROCESSING PORTION (CPU)
15
INTERNAL DATABASE (DB)
16
DISPLAY PORTION
10

FIG. 26

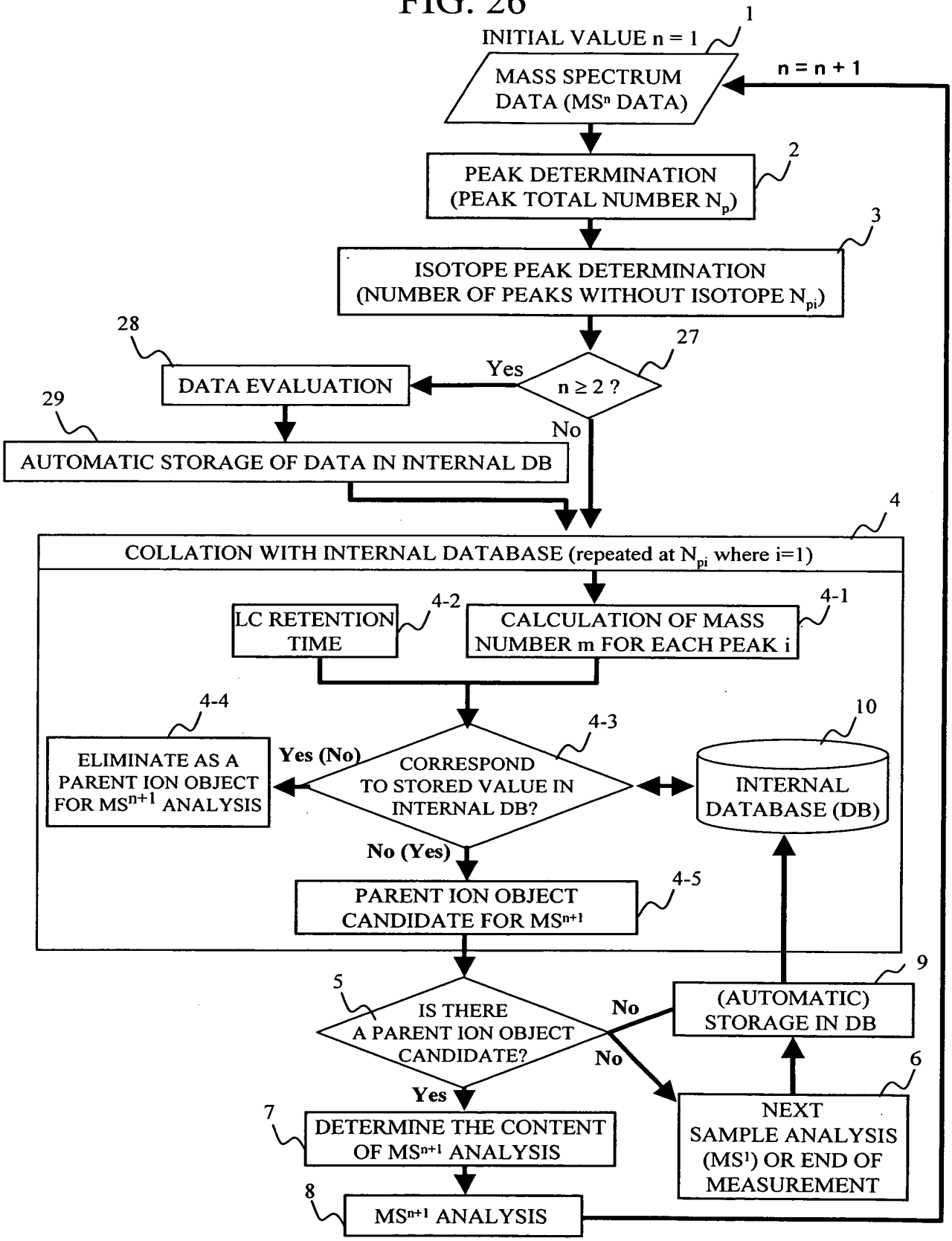

1
INITIAL VALUE n = 1
MASS SPECTRUM DATA (MSⁿ DATA)
n = n + 1
2
PEAK DETERMINATION (PEAK TOTAL NUMBER N_p)
3
ISOTOPE PEAK DETERMINATION (NUMBER OF PEAKS WITHOUT ISOTOPE N_{pi})
28
DATA EVALUATION
Yes
27
n ≥ 2 ?
No
29
AUTOMATIC STORAGE OF DATA IN INTERNAL DB
4
COLLATION WITH INTERNAL DATABASE (repeated at N_{pi} where i=1)
4-2
LC RETENTION TIME
4-1
CALCULATION OF MASS NUMBER m FOR EACH PEAK i
4-4
ELIMINATE AS A PARENT ION OBJECT FOR MS^n+1 ANALYSIS
Yes (No)
4-3
CORRESPOND TO STORED VALUE IN INTERNAL DB?
10
INTERNAL DATABASE (DB)
No (Yes)
4-5
PARENT ION OBJECT CANDIDATE FOR MS^n+1
5
IS THERE A PARENT ION OBJECT CANDIDATE?
No
9
(AUTOMATIC) STORAGE IN DB
No
6
NEXT SAMPLE ANALYSIS (MS¹) OR END OF MEASUREMENT
Yes
7
DETERMINE THE CONTENT OF MS^n+1 ANALYSIS
8
MS^n+1 ANALYSIS

FIG. 27

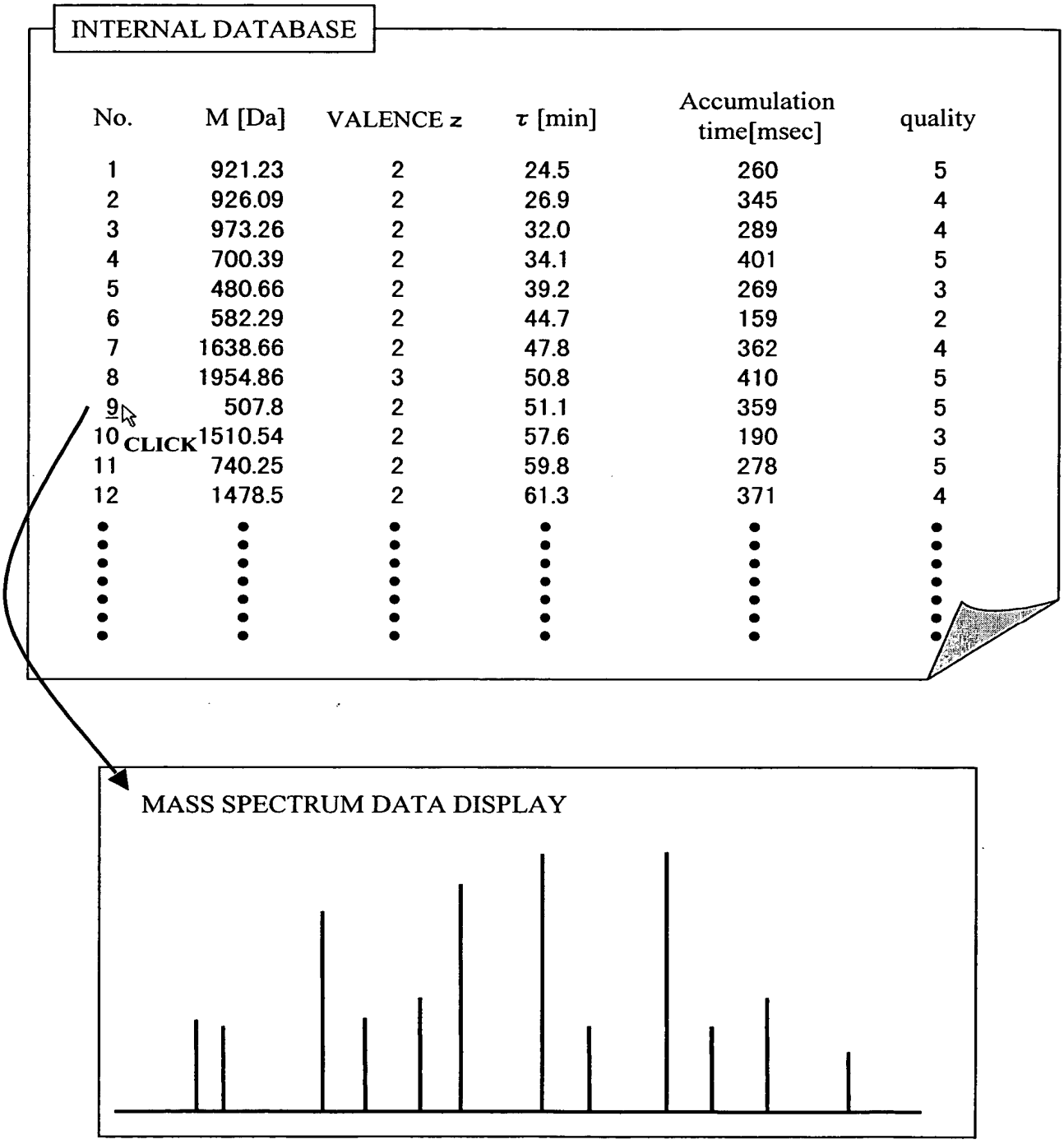

INTERNAL DATABASE
No.
M [Da]
VALENCE z
τ [min]
Accumulation time[msec]
quality
1 921.23 2 24.5 260 5
2 926.09 2 26.9 345 4
3 973.26 2 32.0 289 4
4 700.39 2 34.1 401 5
5 480.66 2 39.2 269 3
6 582.29 2 44.7 159 2
7 1638.66 2 47.8 362 4
8 1954.86 3 50.8 410 5
9 507.8 2 51.1 359 5
10 CLICK 1510.54 2 57.6 190 3
11 740.25 2 59.8 278 5
12 1478.5 2 61.3 371 4
MASS SPECTRUM DATA DISPLAY

FIG. 28 A

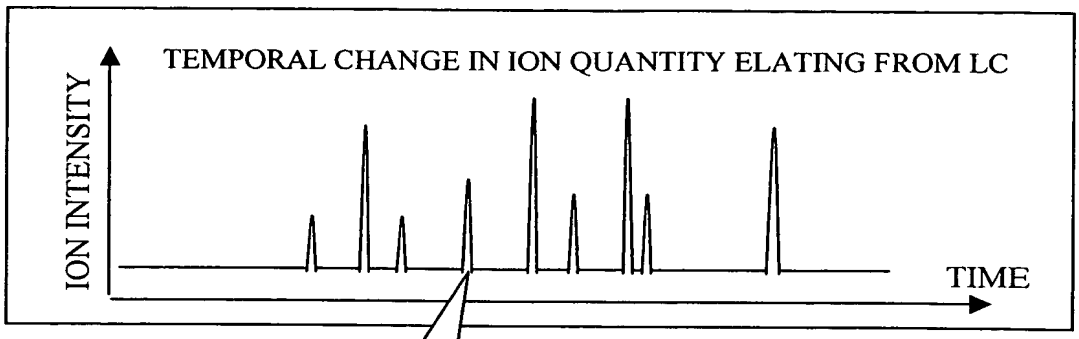


FIG. 28 B

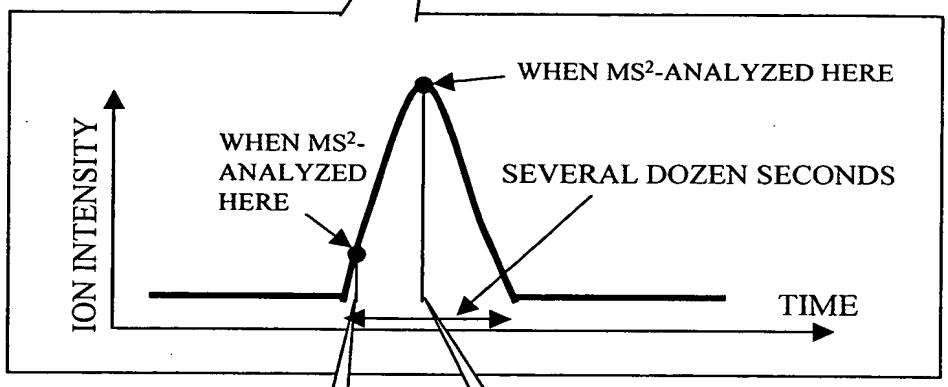


FIG. 28 C

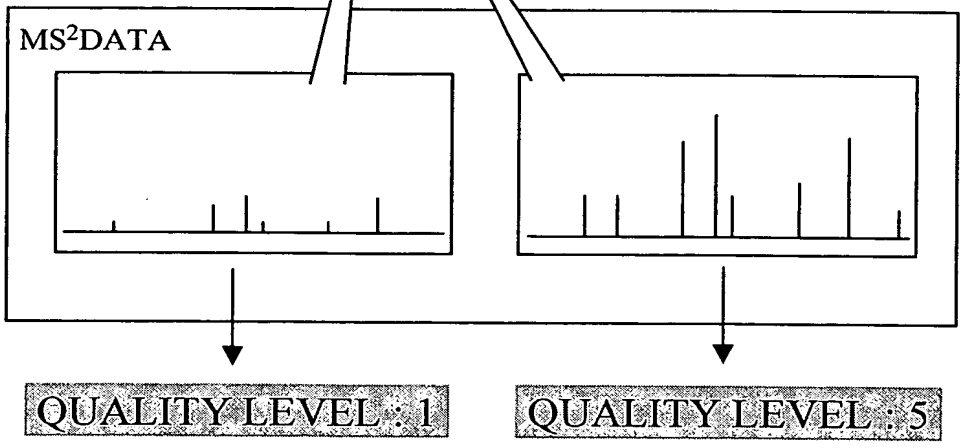


FIG. 29

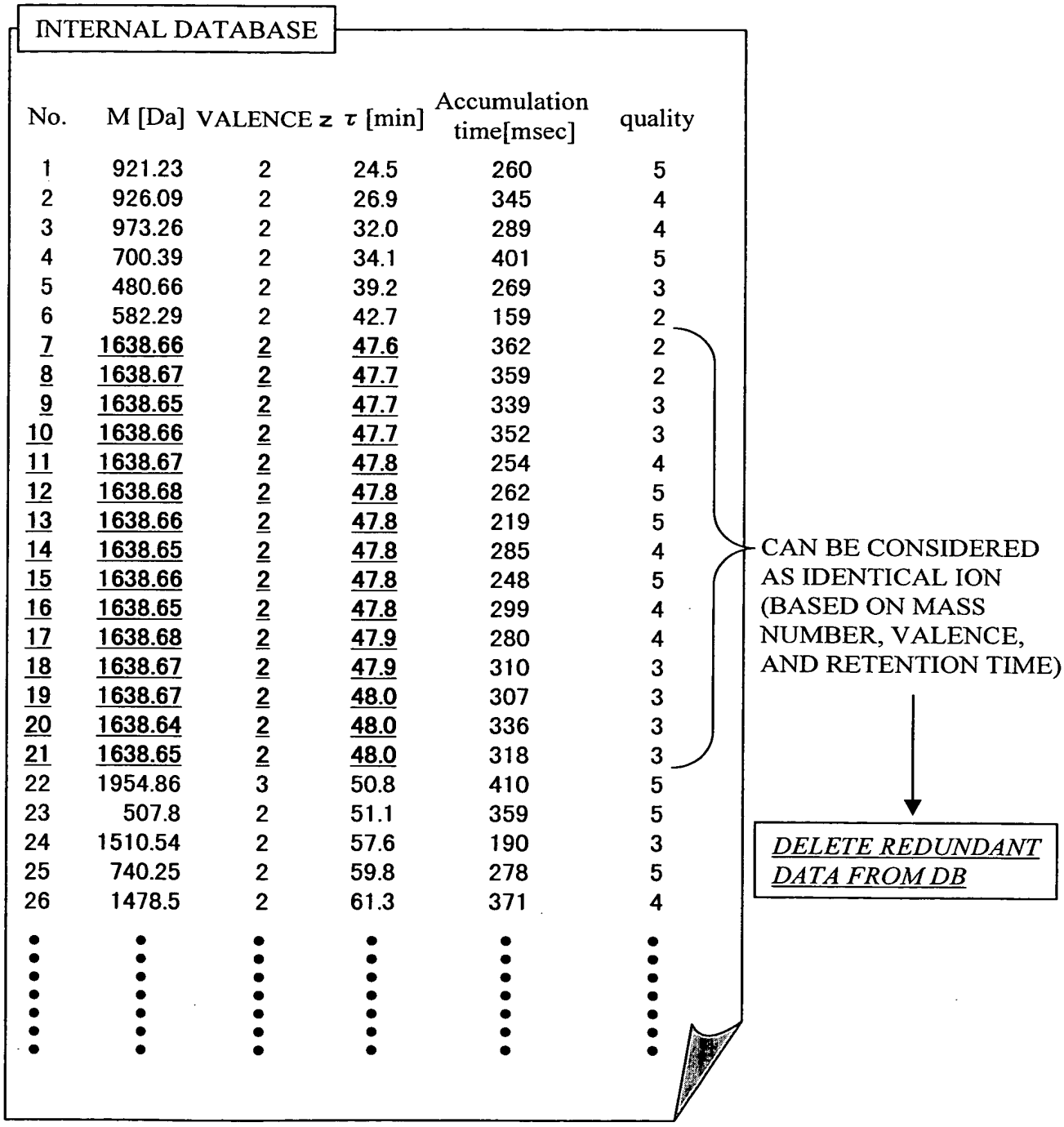

INTERNAL DATABASE
No.
M [Da]
VALENCE z
τ [min]
Accumulation time[msec]
quality
1 921.23 2 24.5 260 5
2 926.09 2 26.9 345 4
3 973.26 2 32.0 289 4
4 700.39 2 34.1 401 5
5 480.66 2 39.2 269 3
6 582.29 2 42.7 159 2
7 1638.66 2 47.6 362 2
8 1638.67 2 47.7 359 2
9 1638.65 2 47.7 339 3
10 1638.66 2 47.7 352 3
11 1638.67 2 47.8 254 4
12 1638.68 2 47.8 262 5
13 1638.66 2 47.8 219 5
14 1638.65 2 47.8 285 4
15 1638.66 2 47.8 248 5
16 1638.65 2 47.8 299 4
17 1638.68 2 47.9 280 4
18 1638.67 2 47.9 310 3
19 1638.67 2 48.0 307 3
20 1638.64 2 48.0 336 3
21 1638.65 2 48.0 318 3
22 1954.86 3 50.8 410 5
23 507.8 2 51.1 359 5
24 1510.54 2 57.6 190 3
25 740.25 2 59.8 278 5
26 1478.5 2 61.3 371 4
CAN BE CONSIDERED AS IDENTICAL ION (BASED ON MASS NUMBER, VALENCE, AND RETENTION TIME)
DELETE REDUNDANT DATA FROM DB

FIG. 30

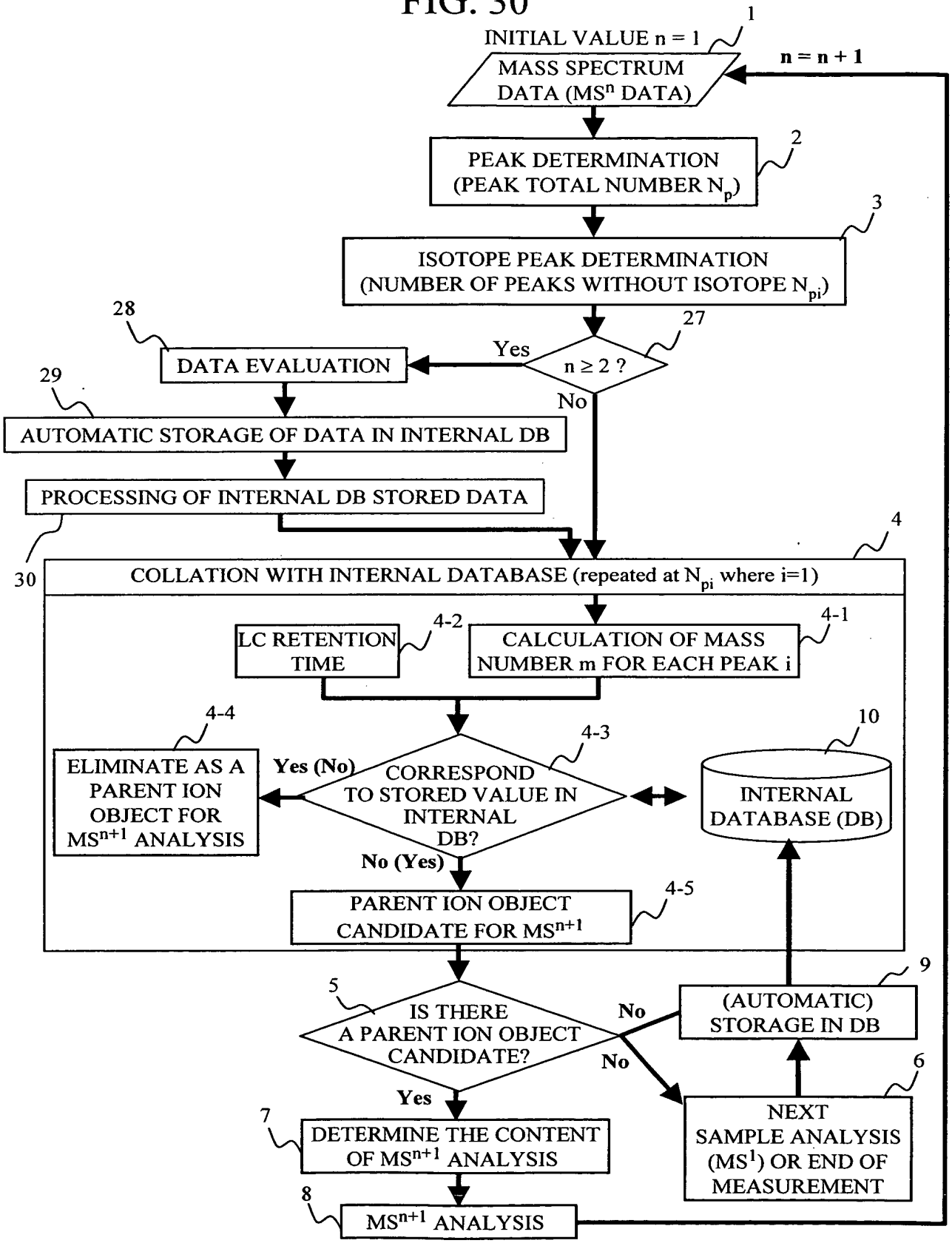

1
INITIAL VALUE n = 1
MASS SPECTRUM DATA (MS^n DATA)
n = n + 1
2
PEAK DETERMINATION (PEAK TOTAL NUMBER N_p)
3
ISOTOPE PEAK DETERMINATION (NUMBER OF PEAKS WITHOUT ISOTOPE N_pi)
27
n ≥ 2 ?
Yes
28
DATA EVALUATION
No
29
AUTOMATIC STORAGE OF DATA IN INTERNAL DB
PROCESSING OF INTERNAL DB STORED DATA
30
4
COLLATION WITH INTERNAL DATABASE (repeated at N_pi where i=1)
4-2
LC RETENTION TIME
4-1
CALCULATION OF MASS NUMBER m FOR EACH PEAK i
4-4
ELIMINATE AS A PARENT ION OBJECT FOR MS^n+1 ANALYSIS
Yes (No)
4-3
CORRESPOND TO STORED VALUE IN INTERNAL DB?
10
INTERNAL DATABASE (DB)
No (Yes)
4-5
PARENT ION OBJECT CANDIDATE FOR MS^n+1
9
5
IS THERE A PARENT ION OBJECT CANDIDATE?
No
(AUTOMATIC) STORAGE IN DB
No
6
Yes
7
DETERMINE THE CONTENT OF MS^n+1 ANALYSIS
NEXT SAMPLE ANALYSIS (MS^1) OR END OF MEASUREMENT
8
MS^n+1 ANALYSIS

FIG. 31

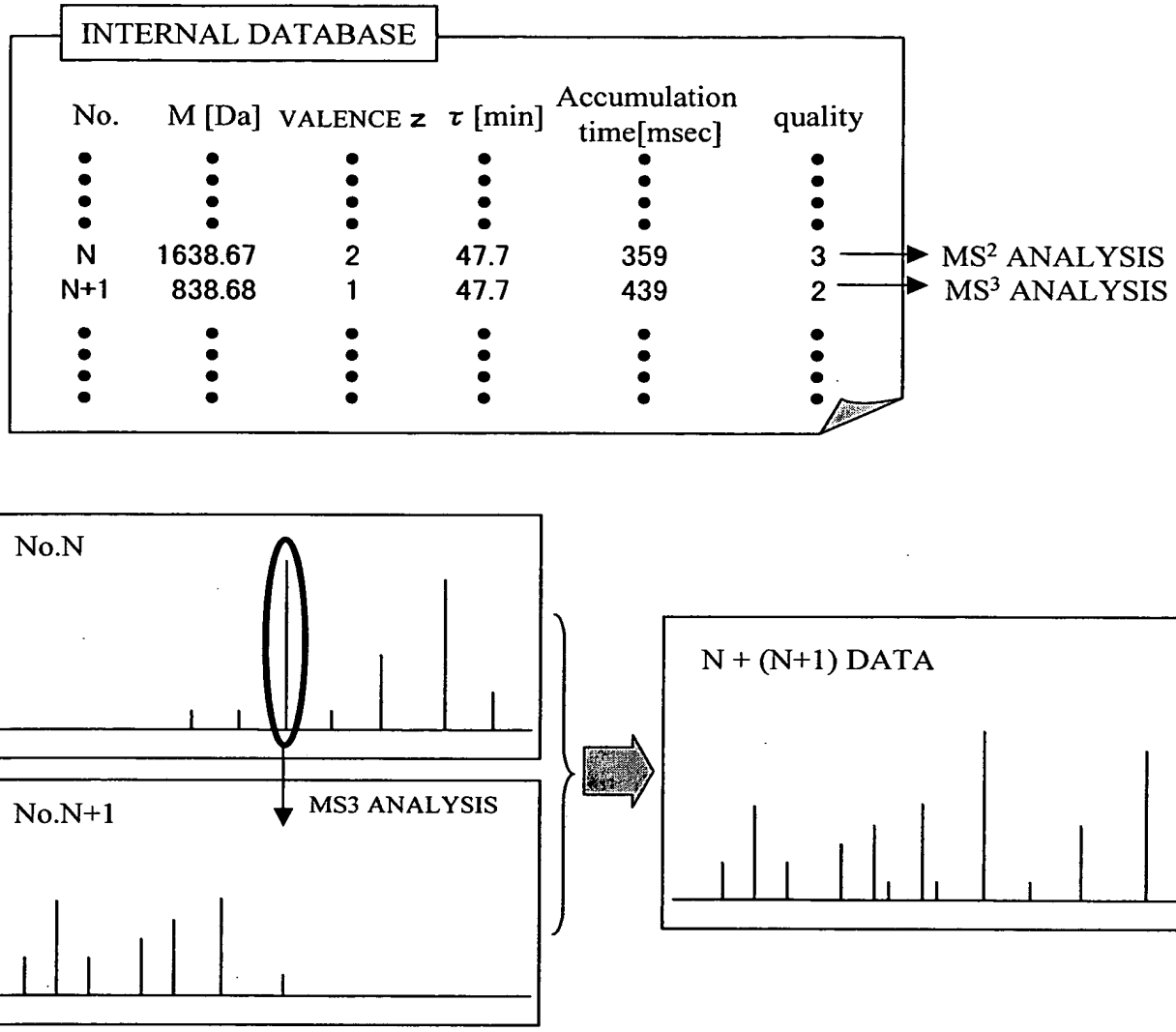

INTERNAL DATABASE
No.
M [Da]
VALENCE z
τ [min]
Accumulation time[msec]
quality
N
1638.67
2
47.7
359
3
MS2 ANALYSIS
N+1
838.68
1
47.7
439
2
MS3 ANALYSIS
No.N
No.N+1
MS3 ANALYSIS
N + (N+1) DATA

FIG. 32

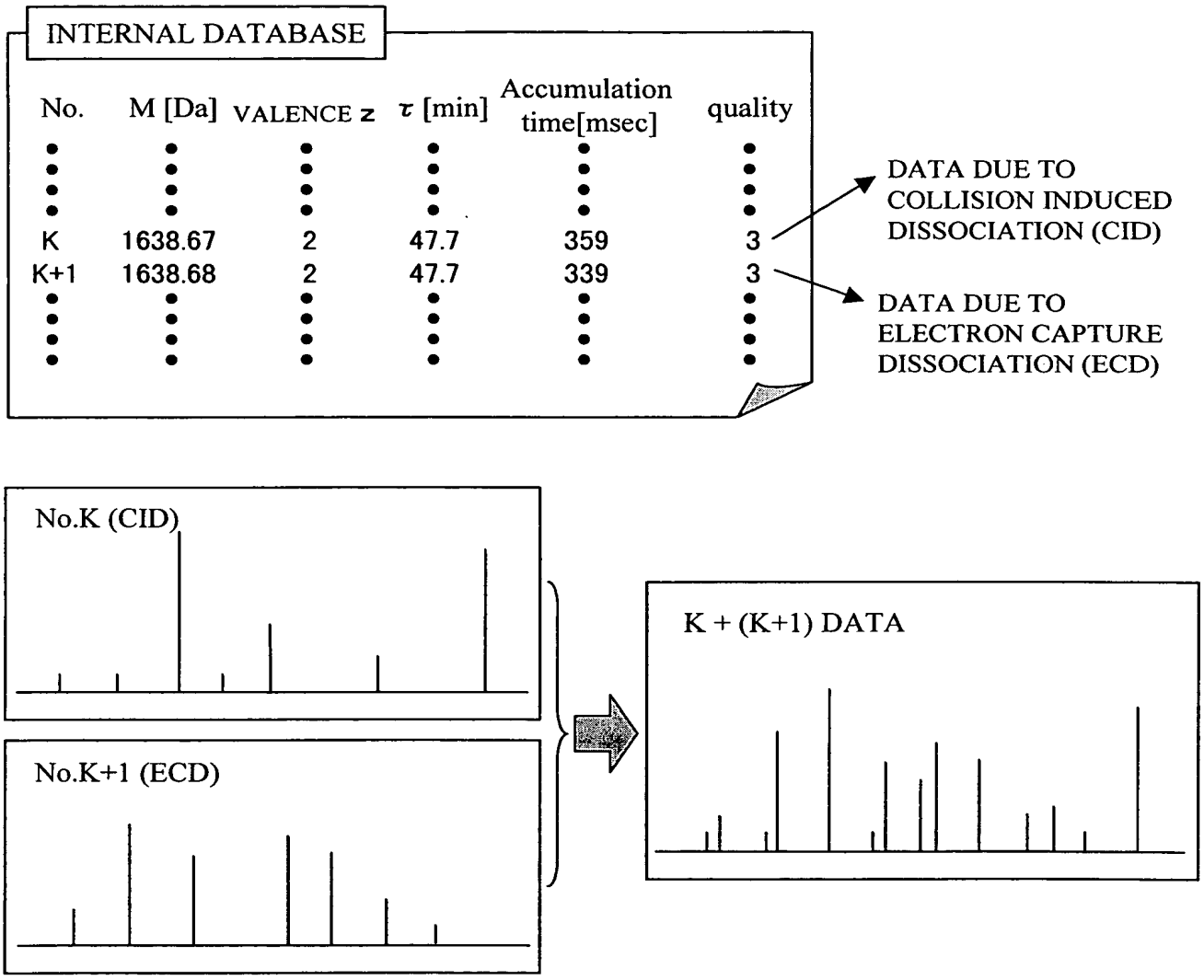

INTERNAL DATABASE
No.
M [Da]
VALENCE z
τ [min]
Accumulation time[msec]
quality
K
1638.67
2
47.7
359
3
K+1
1638.68
2
47.7
339
3
DATA DUE TO COLLISION INDUCED DISSOCIATION (CID)
DATA DUE TO ELECTRON CAPTURE DISSOCIATION (ECD)
No.K (CID)
No.K+1 (ECD)
K + (K+1) DATA

FIG. 33

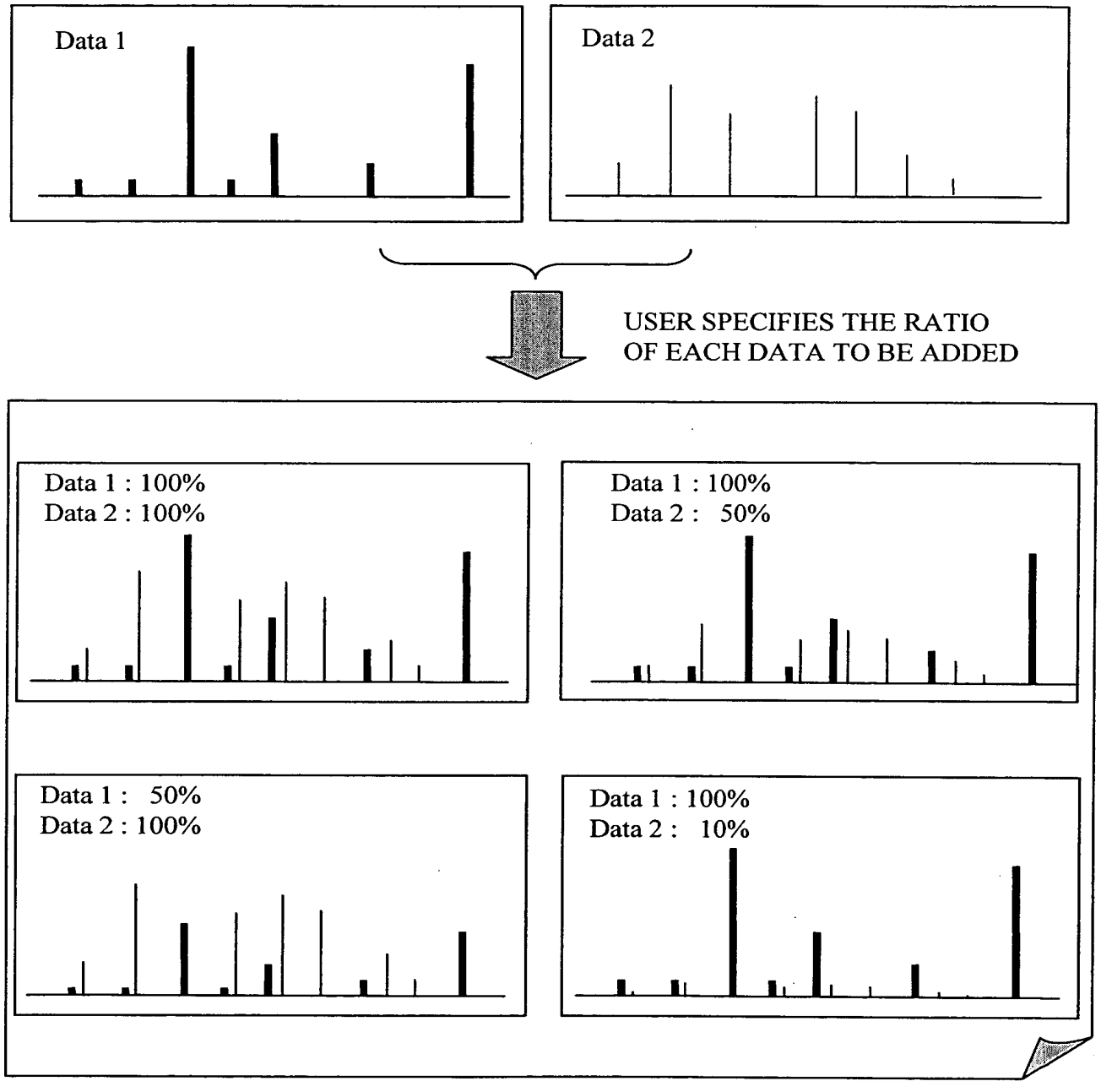

Data 1
Data 2
USER SPECIFIES THE RATIO
OF EACH DATA TO BE ADDED
Data 1 : 100%
Data 2 : 100%
Data 1 : 100%
Data 2 : 50%
Data 1 : 50%
Data 2 : 100%
Data 1 : 100%
Data 2 : 10%

FIG. 34

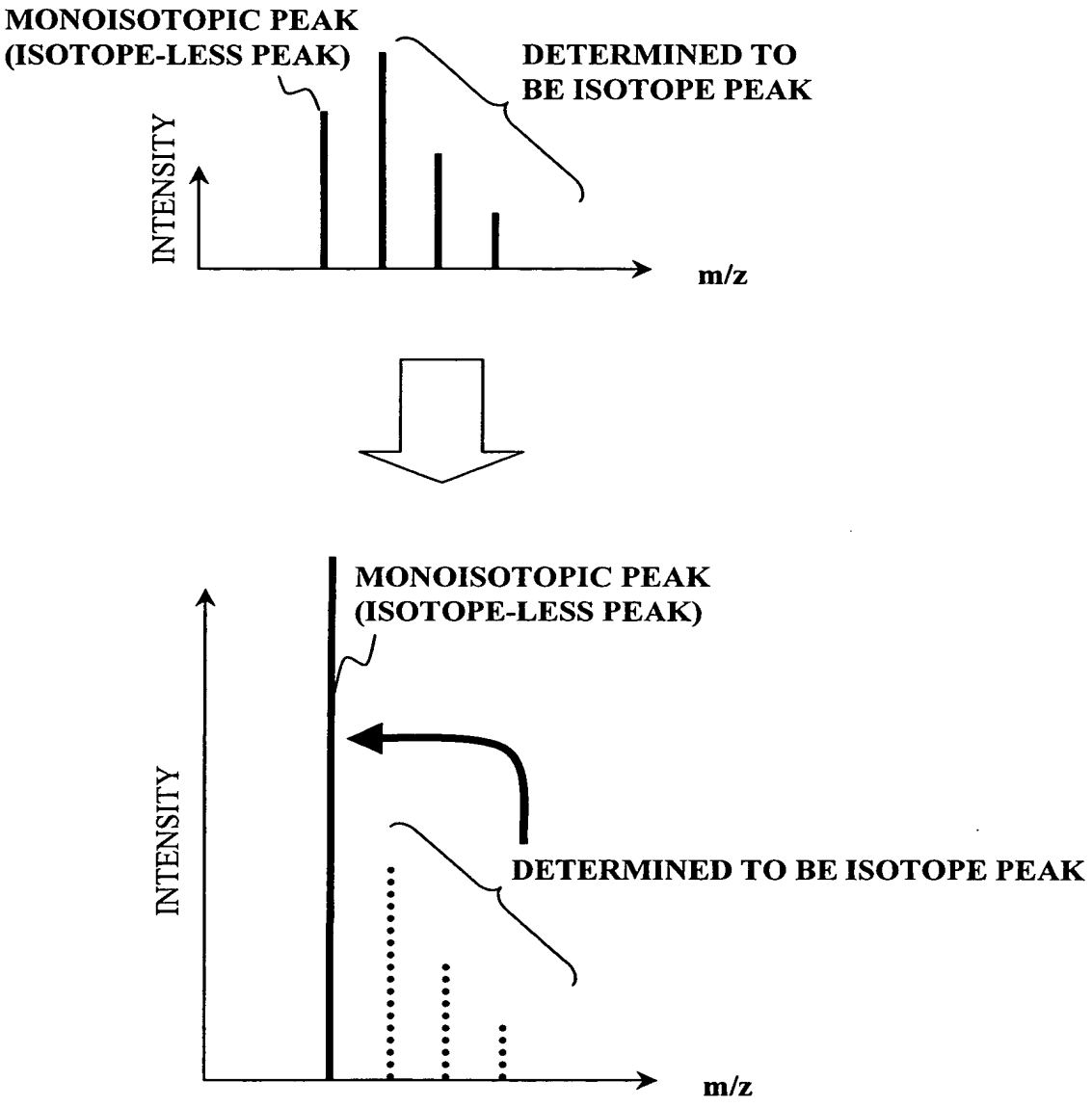

MONOISOTOPIC PEAK
(ISOTOPE-LESS PEAK)
DETERMINED TO
BE ISOTOPE PEAK
INTENSITY
m/z
MONOISOTOPIC PEAK
(ISOTOPE-LESS PEAK)
INTENSITY
DETERMINED TO BE ISOTOPE PEAK
m/z

FIG. 35 a

PROTEIN ANALYSIS AND IDENTIFICATION FLOW IN PRIOR ART

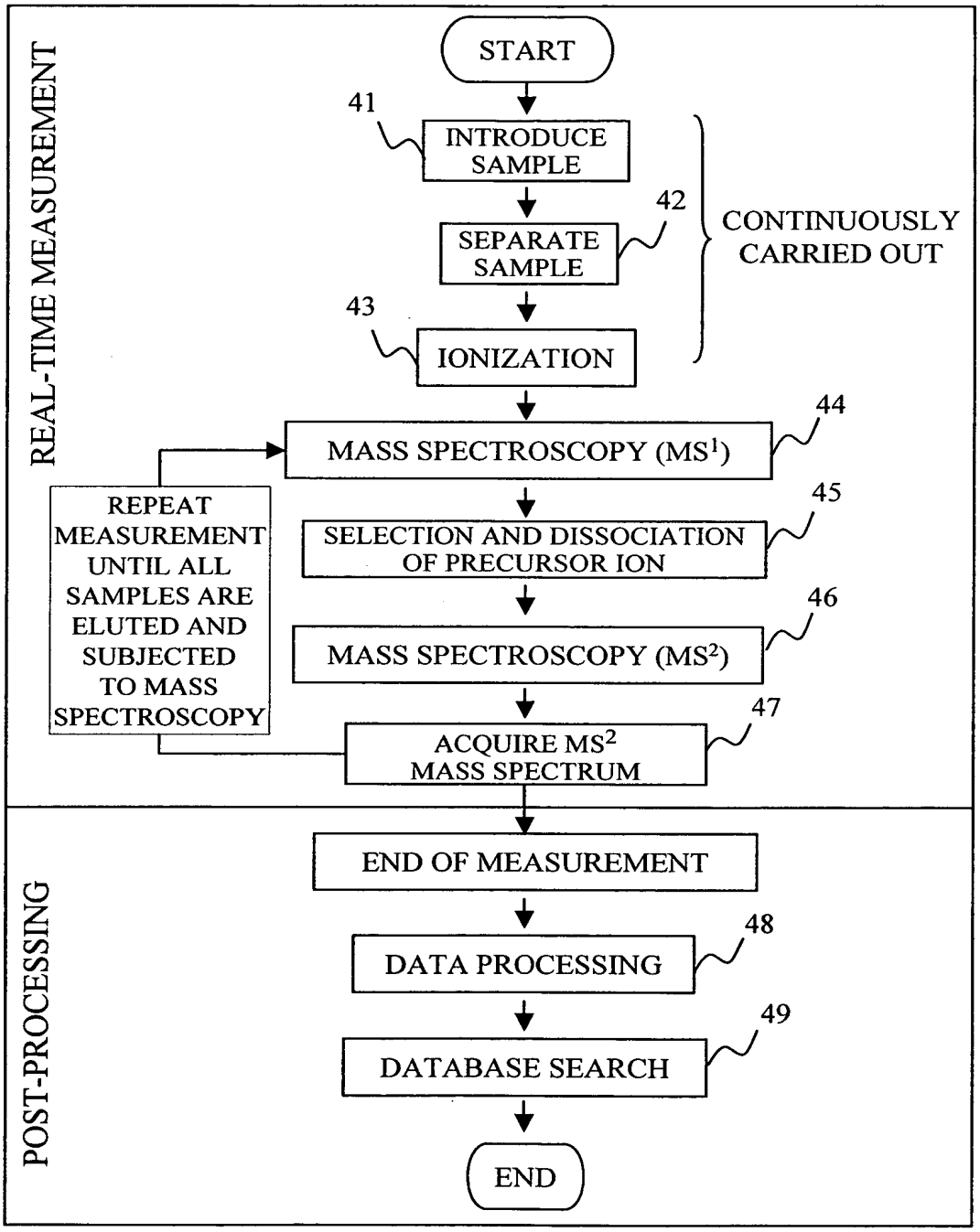


FIG. 35 b

PROTEIN ANALYSIS AND IDENTIFICATION
FLOW IN THE PRESENT EMBODIMENT

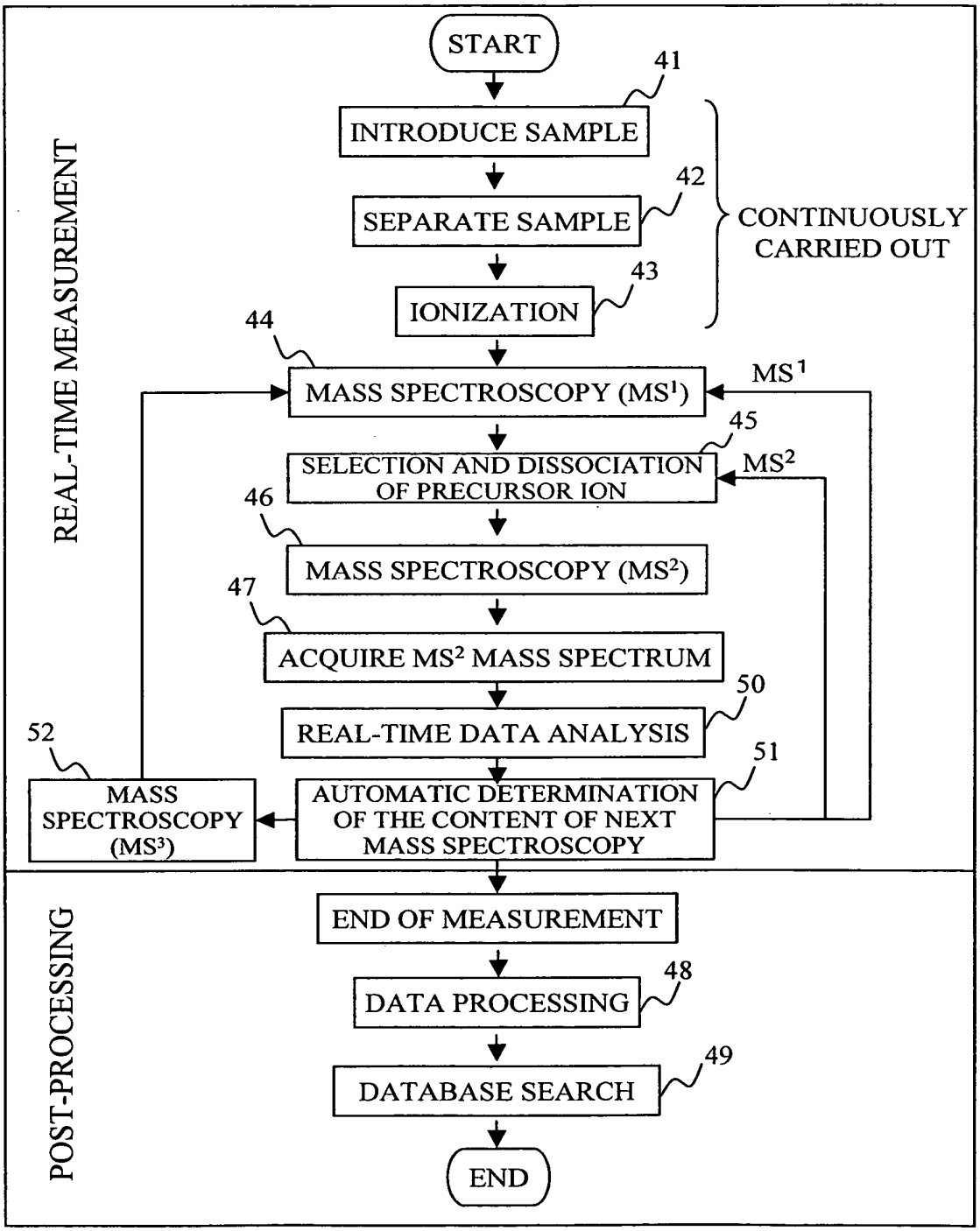


FIG. 36

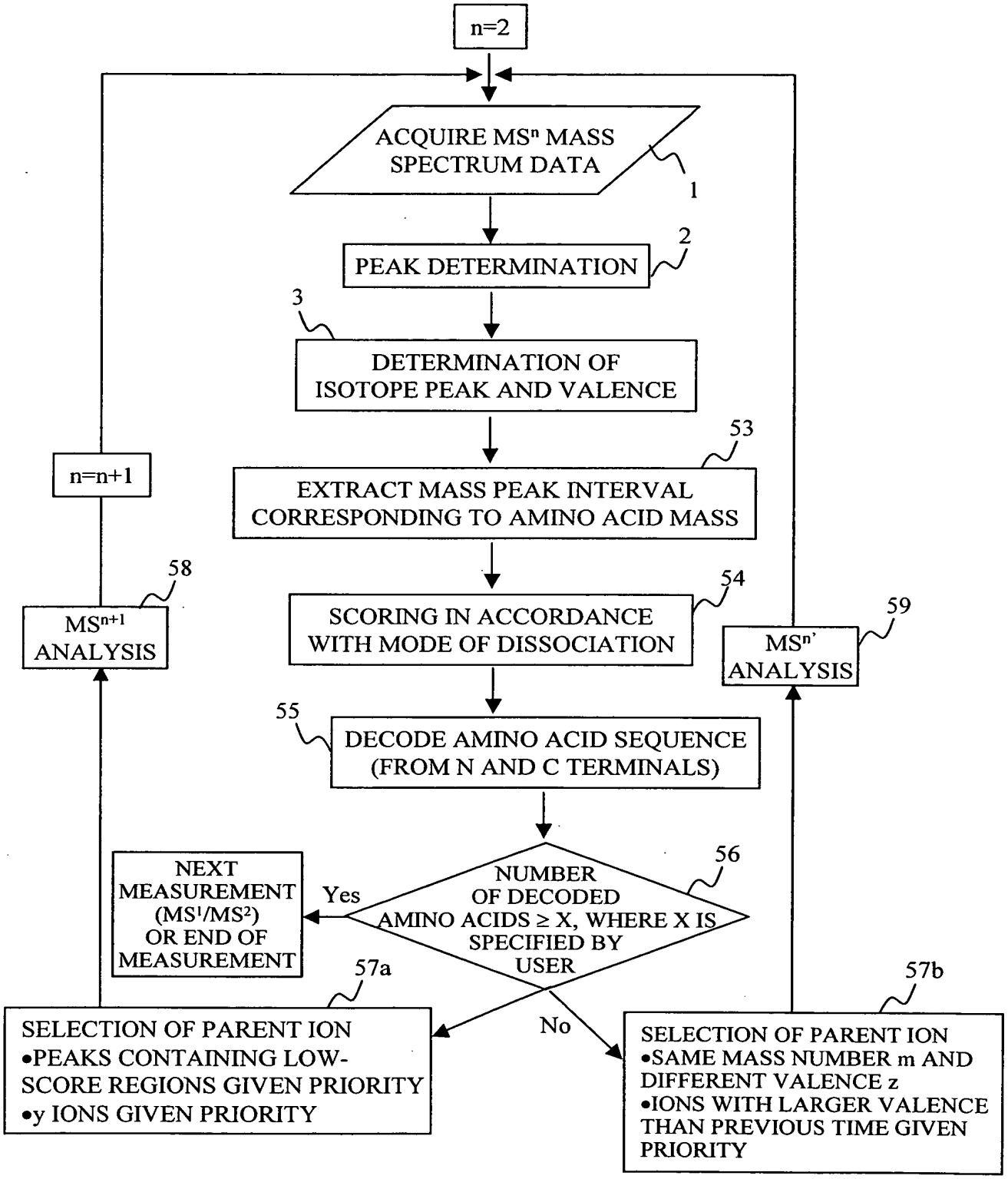

n=2
ACQUIRE MSⁿ MASS SPECTRUM DATA
1
PEAK DETERMINATION
2
3
DETERMINATION OF ISOTOPE PEAK AND VALENCE
53
EXTRACT MASS PEAK INTERVAL CORRESPONDING TO AMINO ACID MASS
54
SCORING IN ACCORDANCE WITH MODE OF DISSOCIATION
55
DECODE AMINO ACID SEQUENCE (FROM N AND C TERMINALS)
56
NUMBER OF DECODED AMINO ACIDS ≥ X, WHERE X IS SPECIFIED BY USER
Yes
NEXT MEASUREMENT (MS¹/MS²) OR END OF MEASUREMENT
No
57a
SELECTION OF PARENT ION
•PEAKS CONTAINING LOW-SCORE REGIONS GIVEN PRIORITY
•y IONS GIVEN PRIORITY
57b
SELECTION OF PARENT ION
•SAME MASS NUMBER m AND DIFFERENT VALENCE z
•IONS WITH LARGER VALENCE THAN PREVIOUS TIME GIVEN PRIORITY
58
MSⁿ⁺¹ ANALYSIS
n=n+1
59
MSⁿ' ANALYSIS

FIG. 37

MIFVGIK

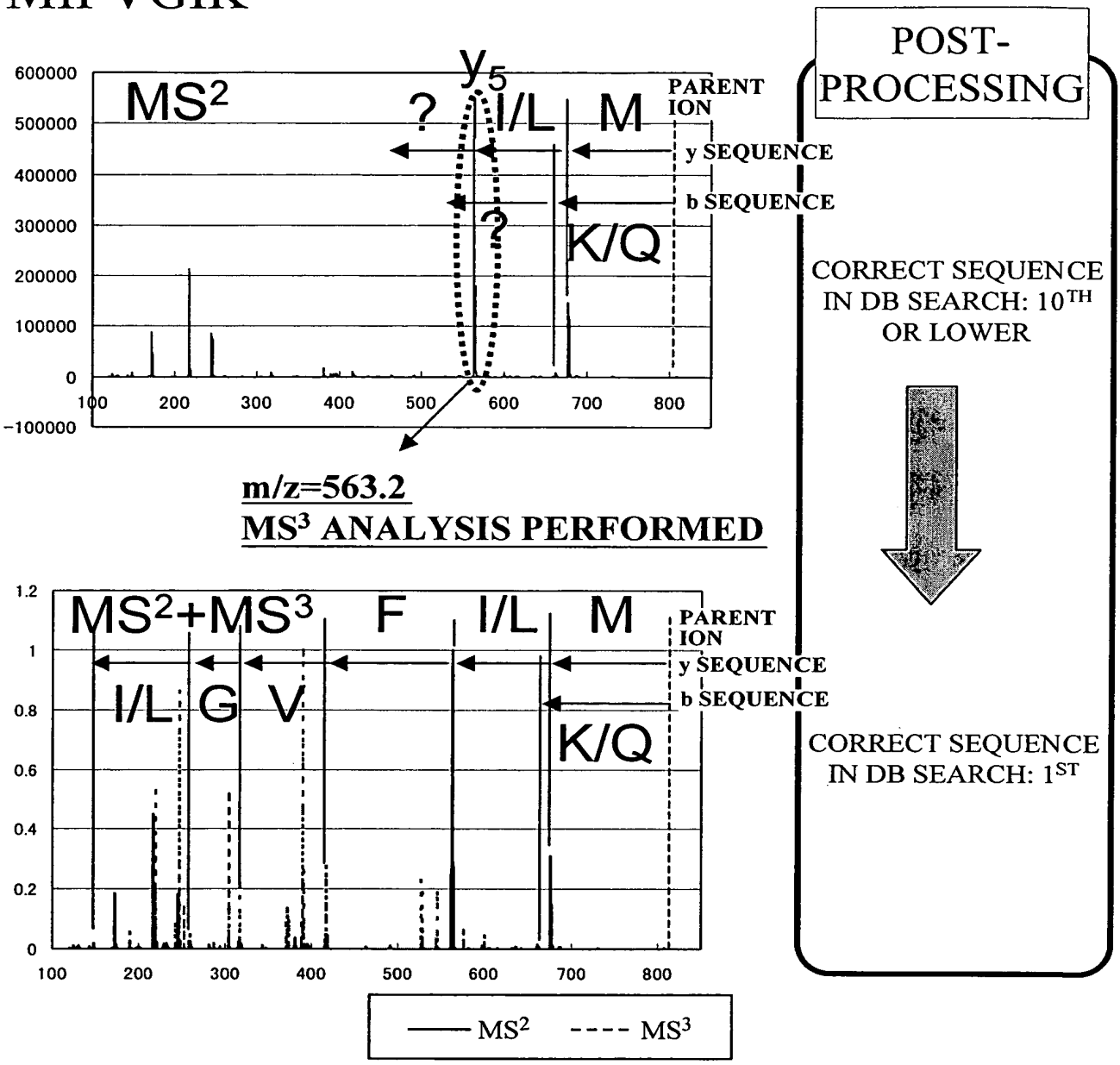


FIG. 38

FLOWCHART (REAL-TIME DB SEARCH)

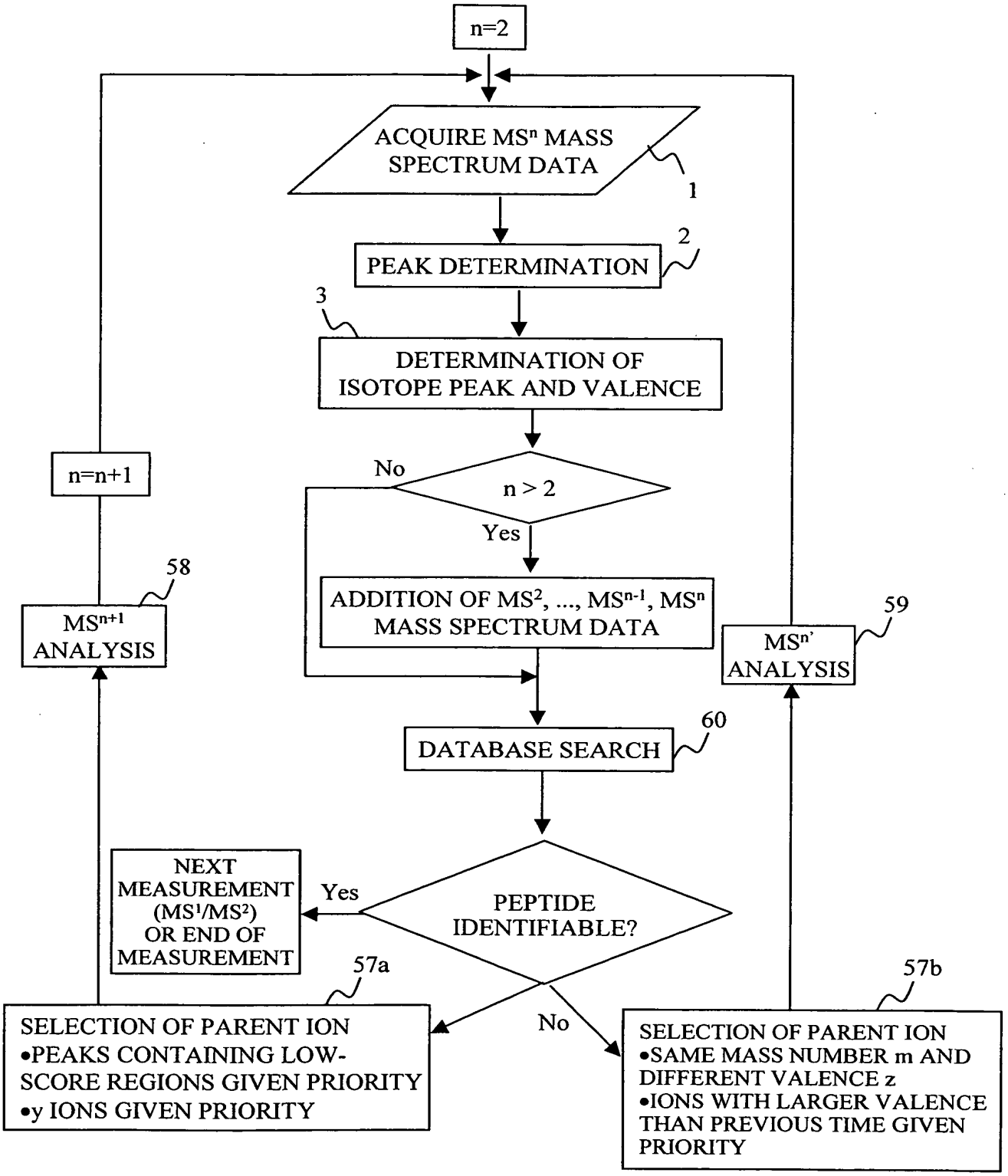


FIG. 39

(FLOWCHAR: SPECIFIC CONDITIONS → MS3/MS2')

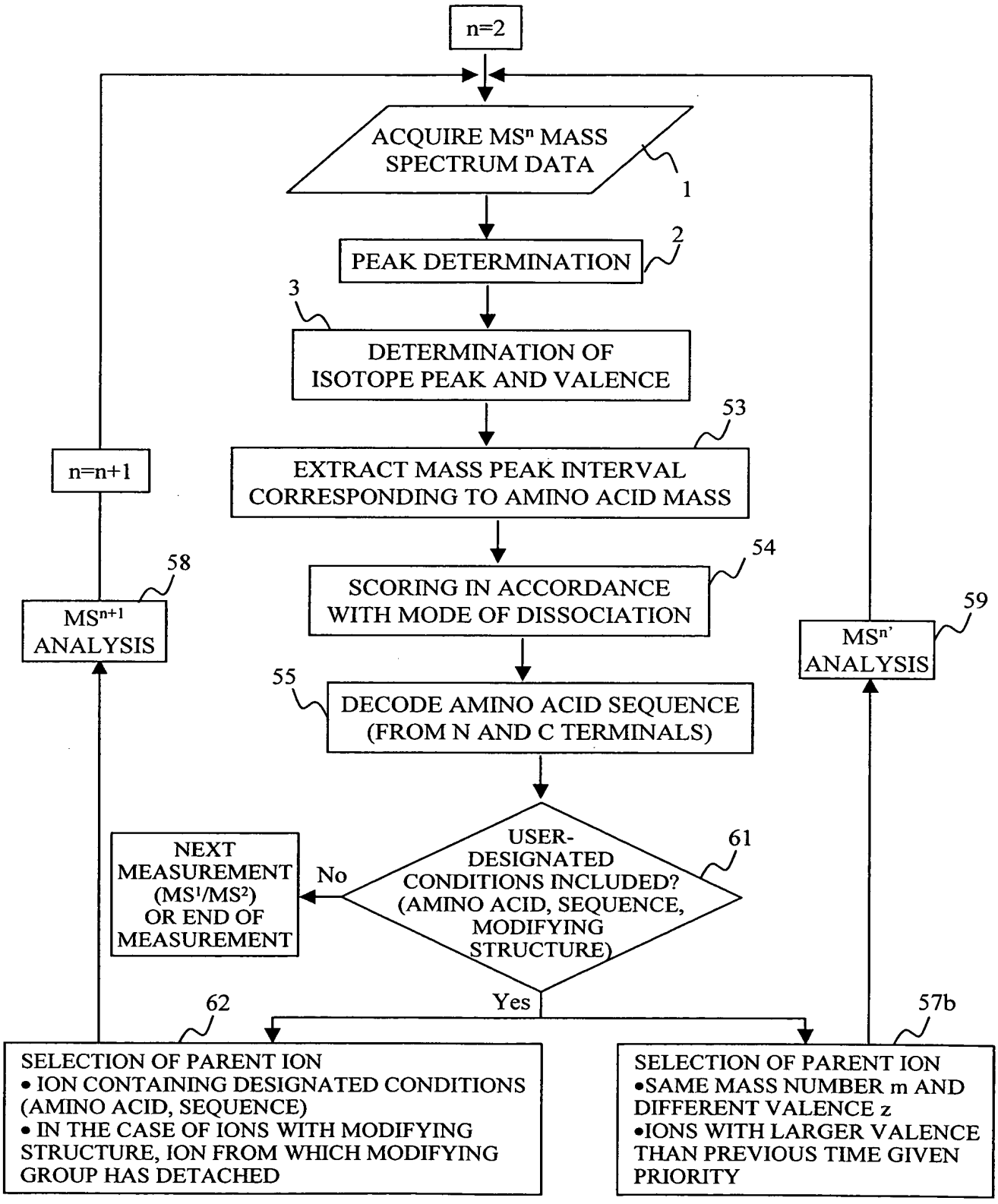


FIG. 40

(DERIVATION OF NUMBER OF PEAK GROUPS)

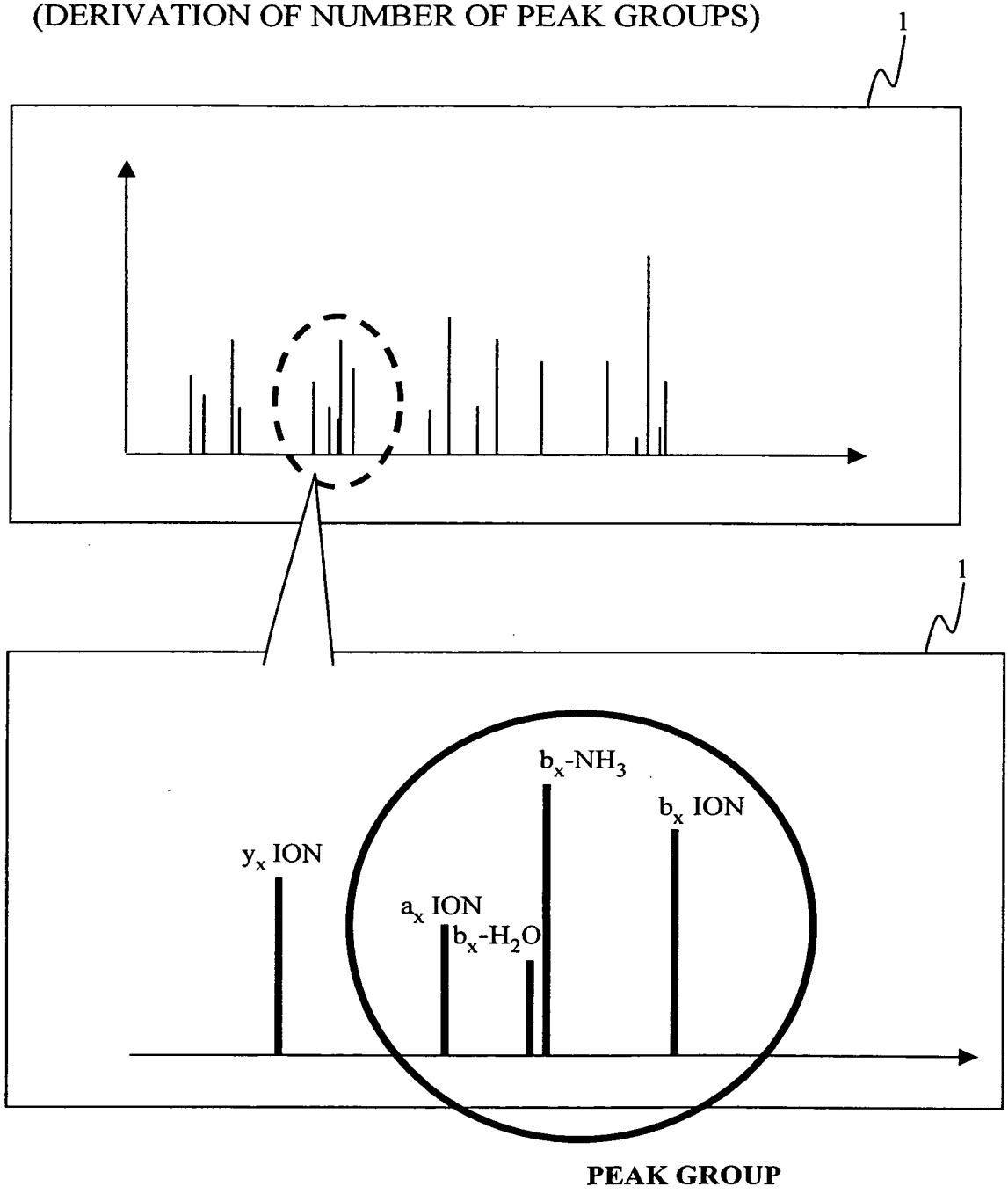


FIG. 41

(FLOWCHART: DETERMINATION BASED ON PEAK GROUP)

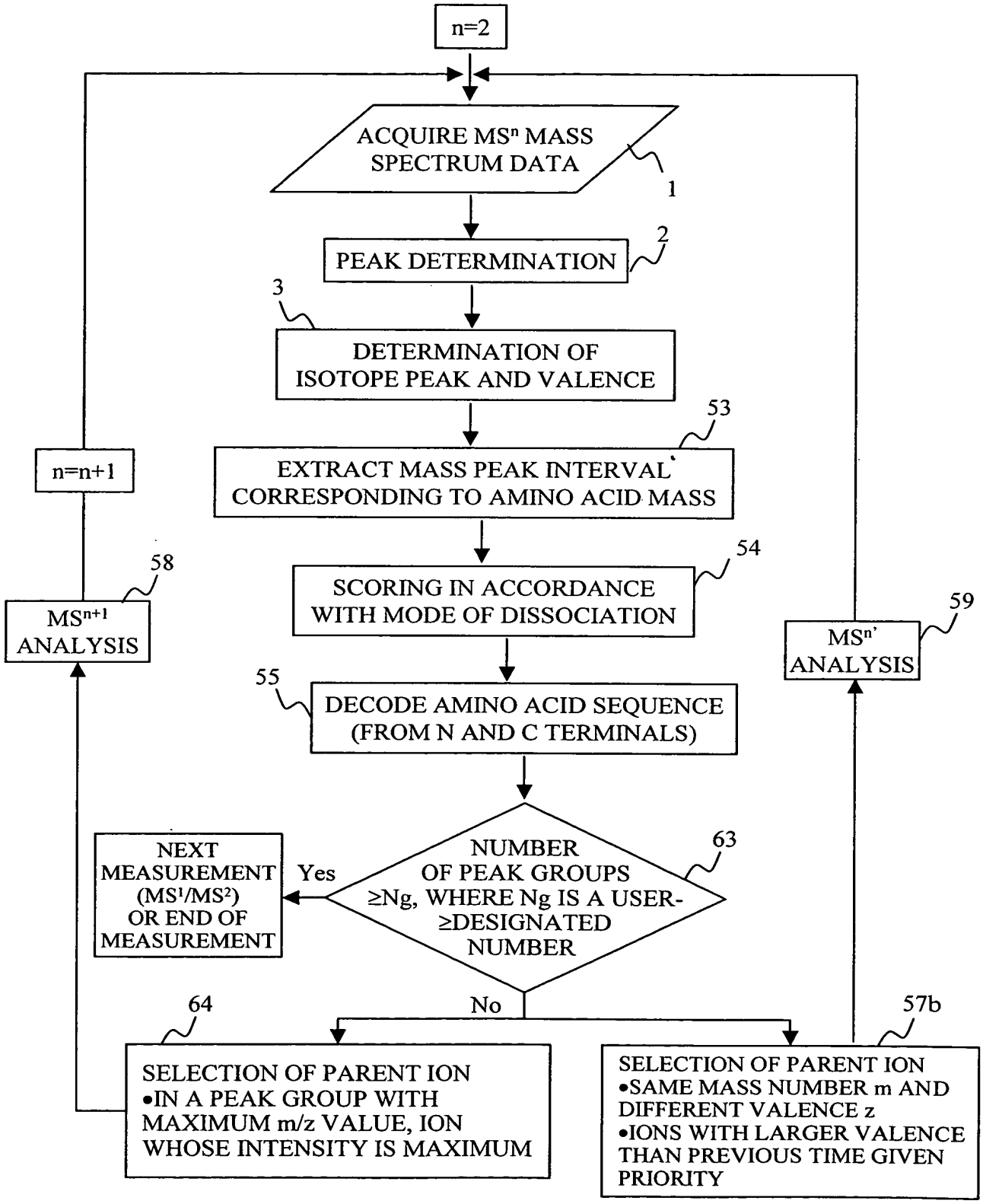


FIG. 42

(FLOWCHART: DETERMINATION BASED ON NUMBER OF PEAKS)

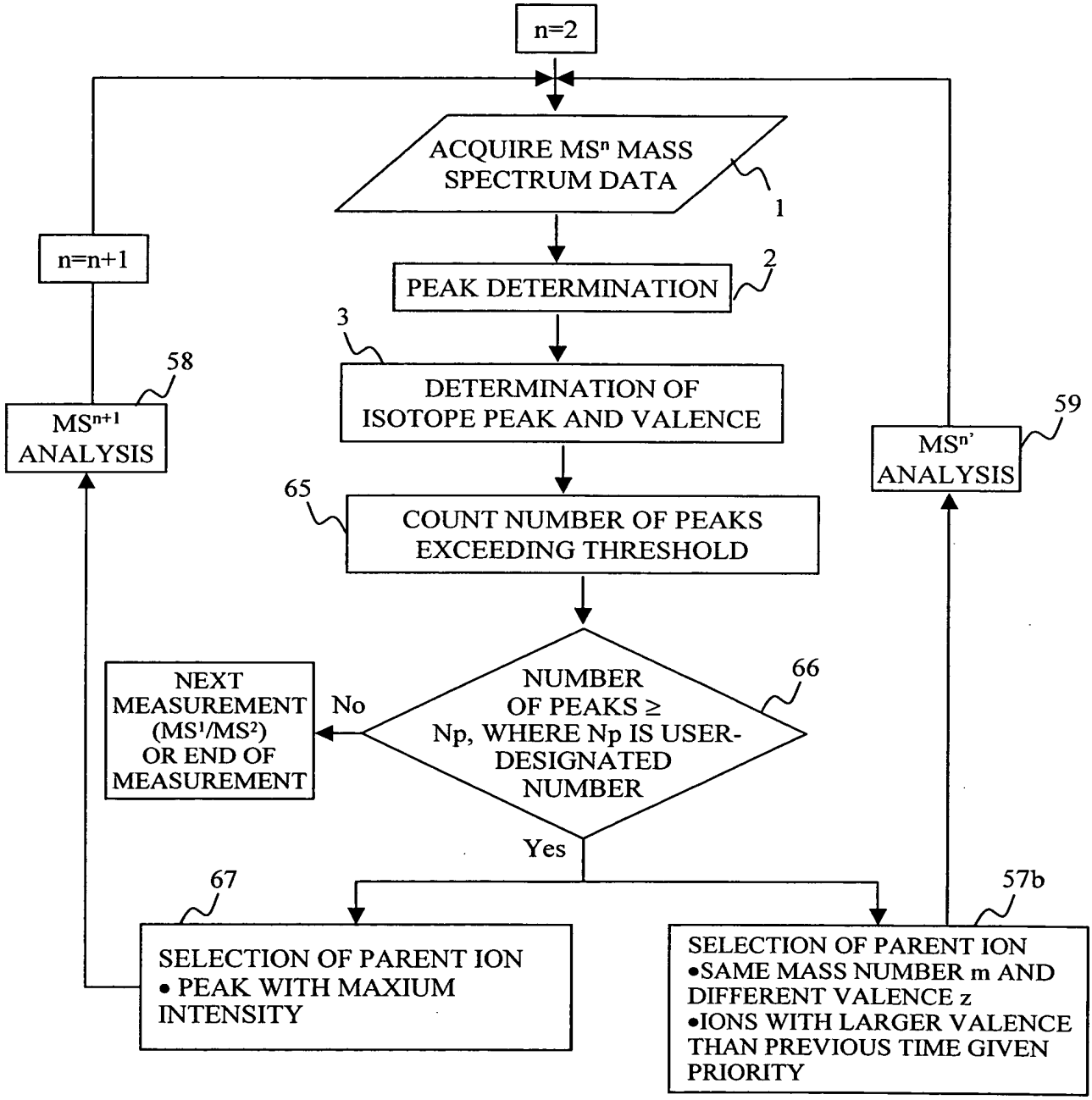


FIG. 43

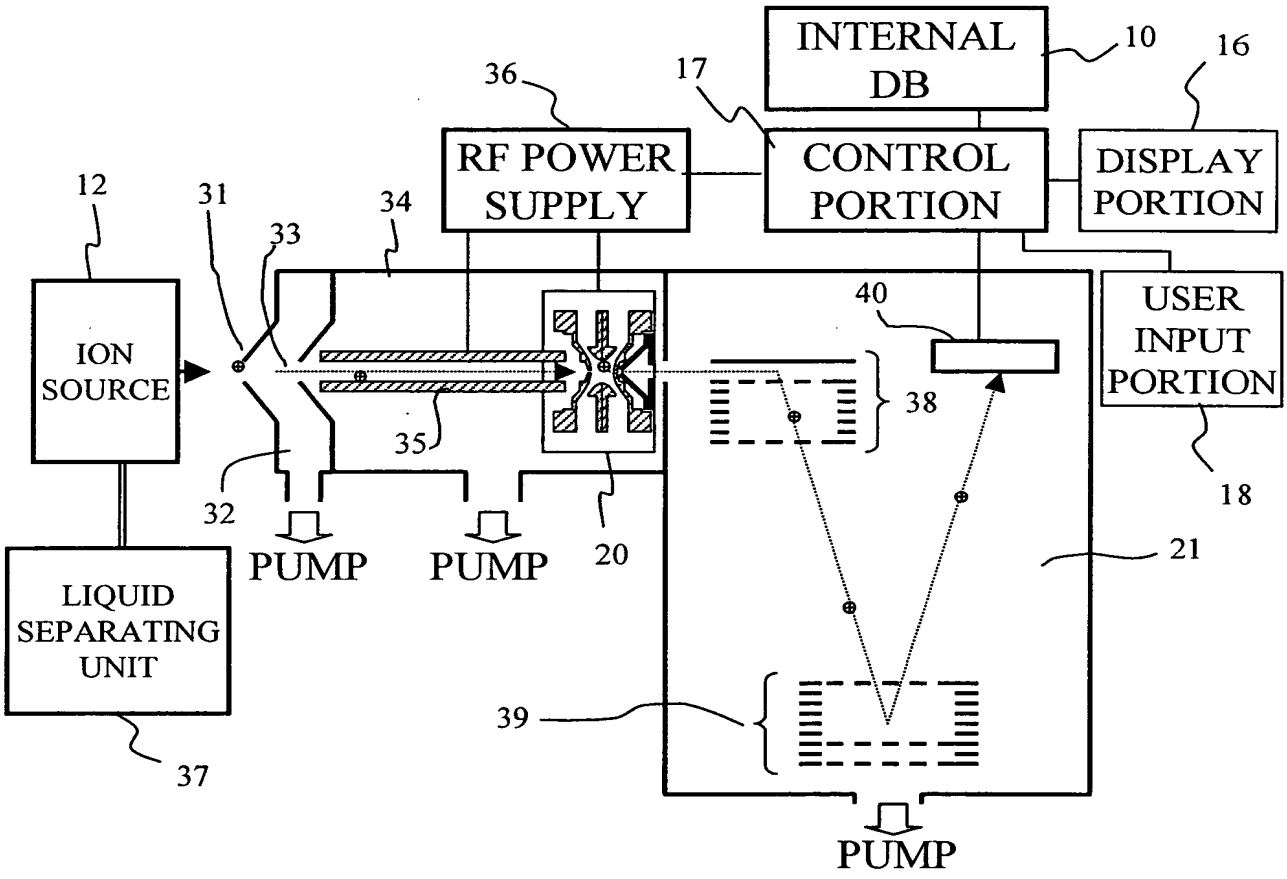

INTERNAL DB
10
16
36
17
RF POWER SUPPLY
CONTROL PORTION
DISPLAY PORTION
12
31
33
34
ION SOURCE
40
USER INPUT PORTION
38
35
18
32
PUMP
PUMP
20
21
LIQUID SEPARATING UNIT
39
37
PUMP

FIG. 44

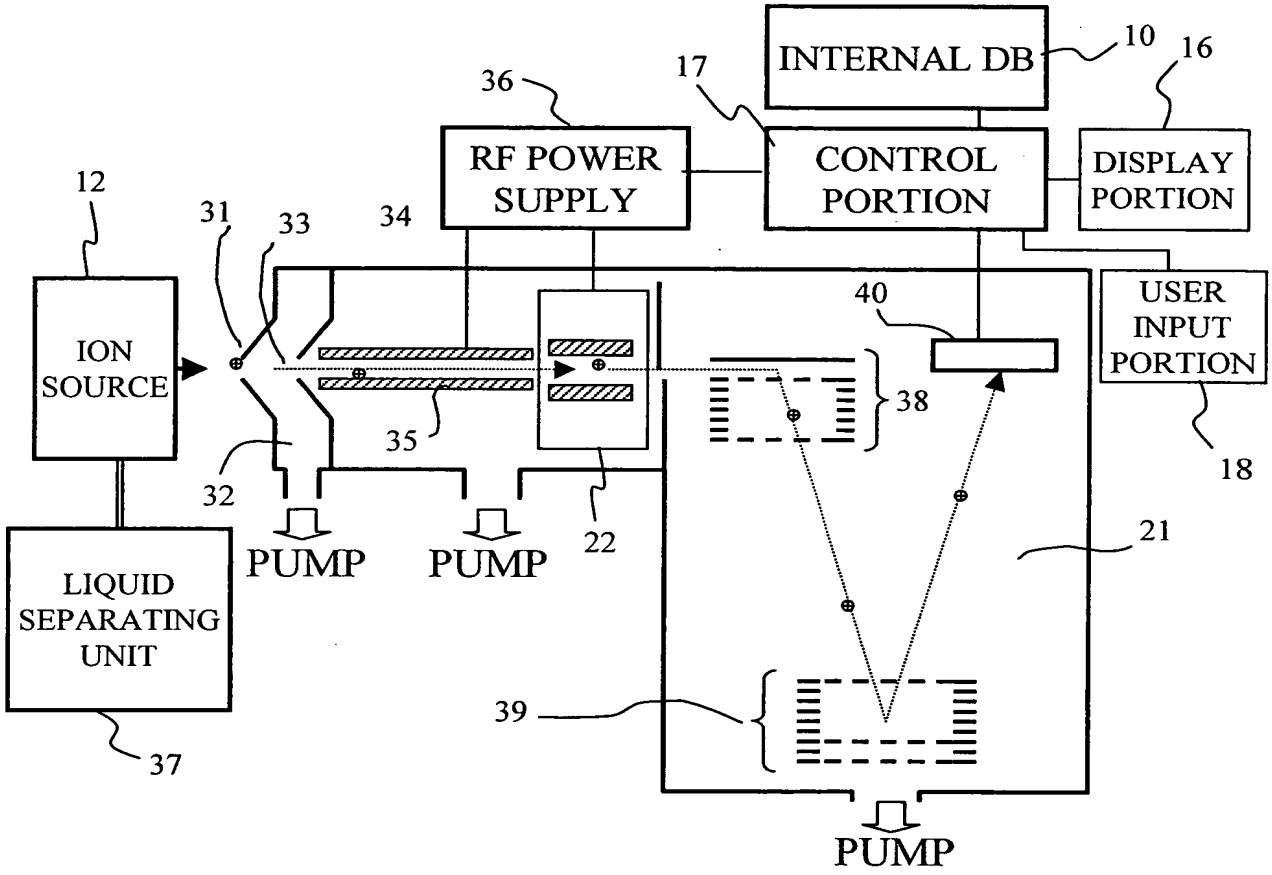

INTERNAL DB
10
16
17
36
RF POWER SUPPLY
CONTROL PORTION
DISPLAY PORTION
12
31
33
34
40
USER INPUT PORTION
ION SOURCE
38
35
18
32
22
21
PUMP
PUMP
LIQUID SEPARATING UNIT
39
37
PUMP

FIG. 45

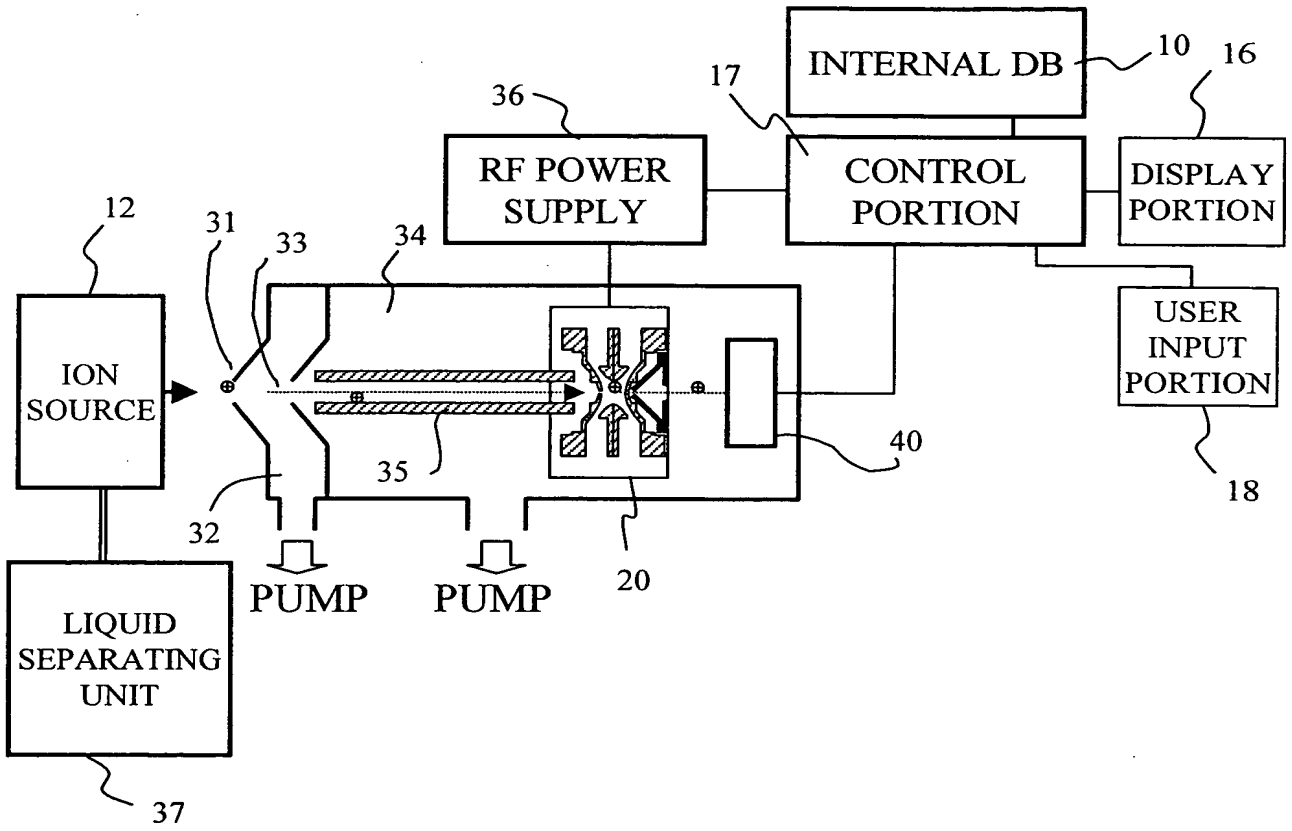

INTERNAL DB
10
16
17
36
RF POWER SUPPLY
CONTROL PORTION
DISPLAY PORTION
12
31
33
34
ION SOURCE
USER INPUT PORTION
40
35
18
32
PUMP
PUMP
20
LIQUID SEPARATING UNIT
37

FIG. 46

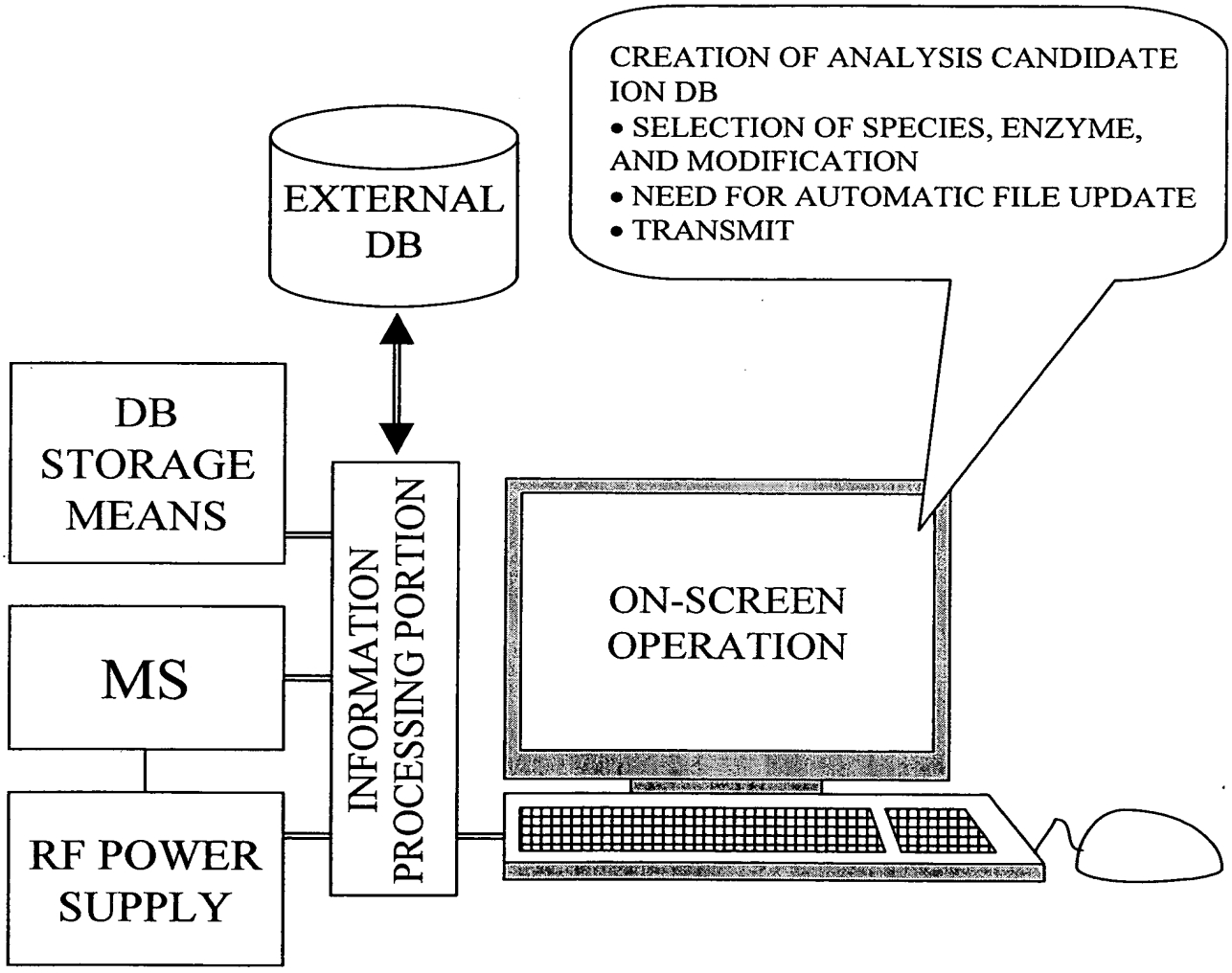

CREATION OF ANALYSIS CANDIDATE ION DB
• SELECTION OF SPECIES, ENZYME, AND MODIFICATION
• NEED FOR AUTOMATIC FILE UPDATE
• TRANSMIT
EXTERNAL DB
DB STORAGE MEANS
MS
RF POWER SUPPLY
INFORMATION PROCESSING PORTION
ON-SCREEN OPERATION

FIG. 47

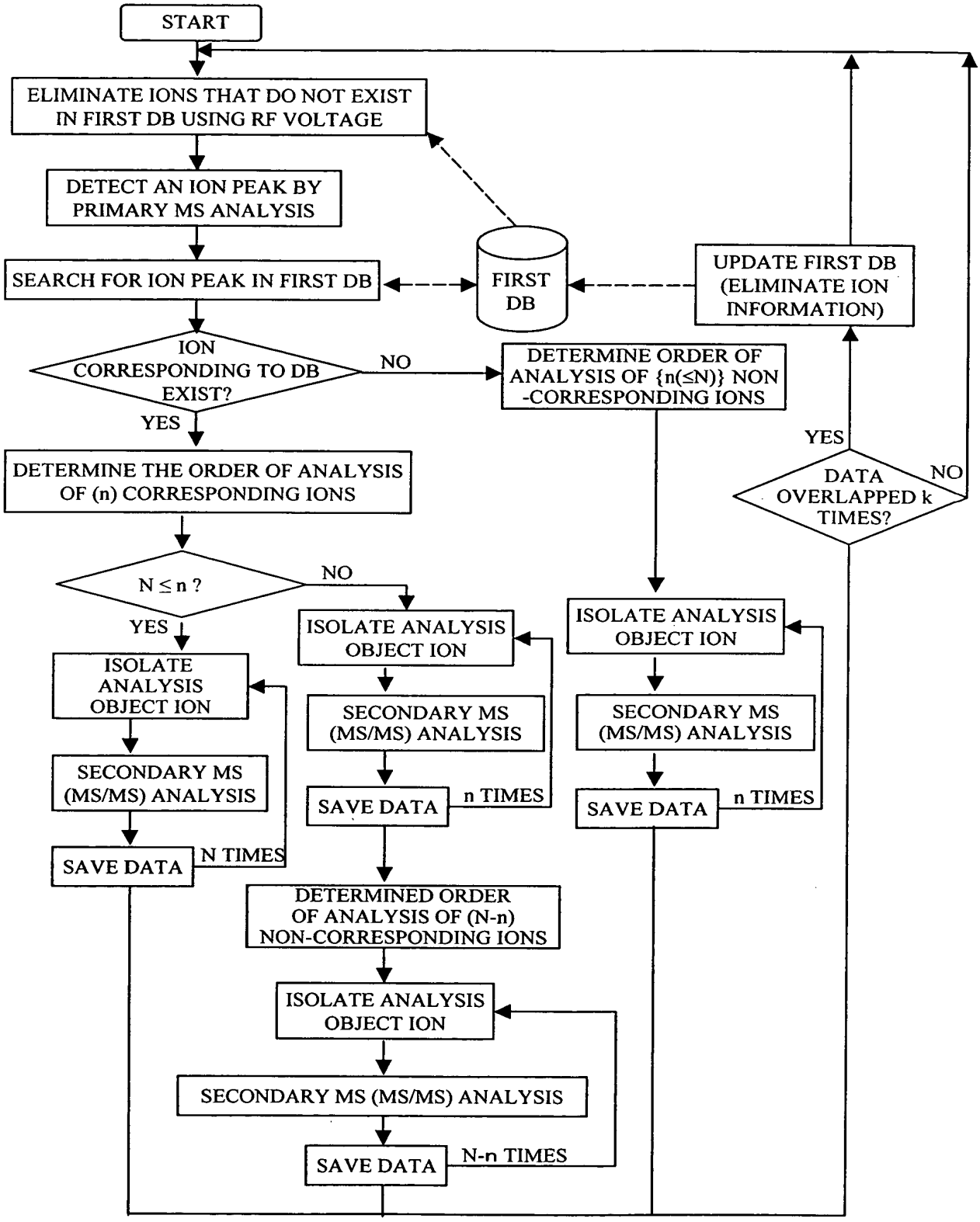

START
ELIMINATE IONS THAT DO NOT EXIST IN FIRST DB USING RF VOLTAGE
DETECT AN ION PEAK BY PRIMARY MS ANALYSIS
SEARCH FOR ION PEAK IN FIRST DB
FIRST DB
UPDATE FIRST DB (ELIMINATE ION INFORMATION)
ION CORRESPONDING TO DB EXIST?
NO
DETERMINE ORDER OF ANALYSIS OF {n(≤N)} NON -CORRESPONDING IONS
YES
DETERMINE THE ORDER OF ANALYSIS OF (n) CORRESPONDING IONS
YES
DATA OVERLAPPED k TIMES?
NO
N ≤ n ?
NO
YES
ISOLATE ANALYSIS OBJECT ION
SECONDARY MS (MS/MS) ANALYSIS
SAVE DATA
N TIMES
ISOLATE ANALYSIS OBJECT ION
SECONDARY MS (MS/MS) ANALYSIS
SAVE DATA
n TIMES
ISOLATE ANALYSIS OBJECT ION
SECONDARY MS (MS/MS) ANALYSIS
SAVE DATA
n TIMES
DETERMINED ORDER OF ANALYSIS OF (N-n) NON-CORRESPONDING IONS
ISOLATE ANALYSIS OBJECT ION
SECONDARY MS (MS/MS) ANALYSIS
SAVE DATA
N-n TIMES

FIG. 48

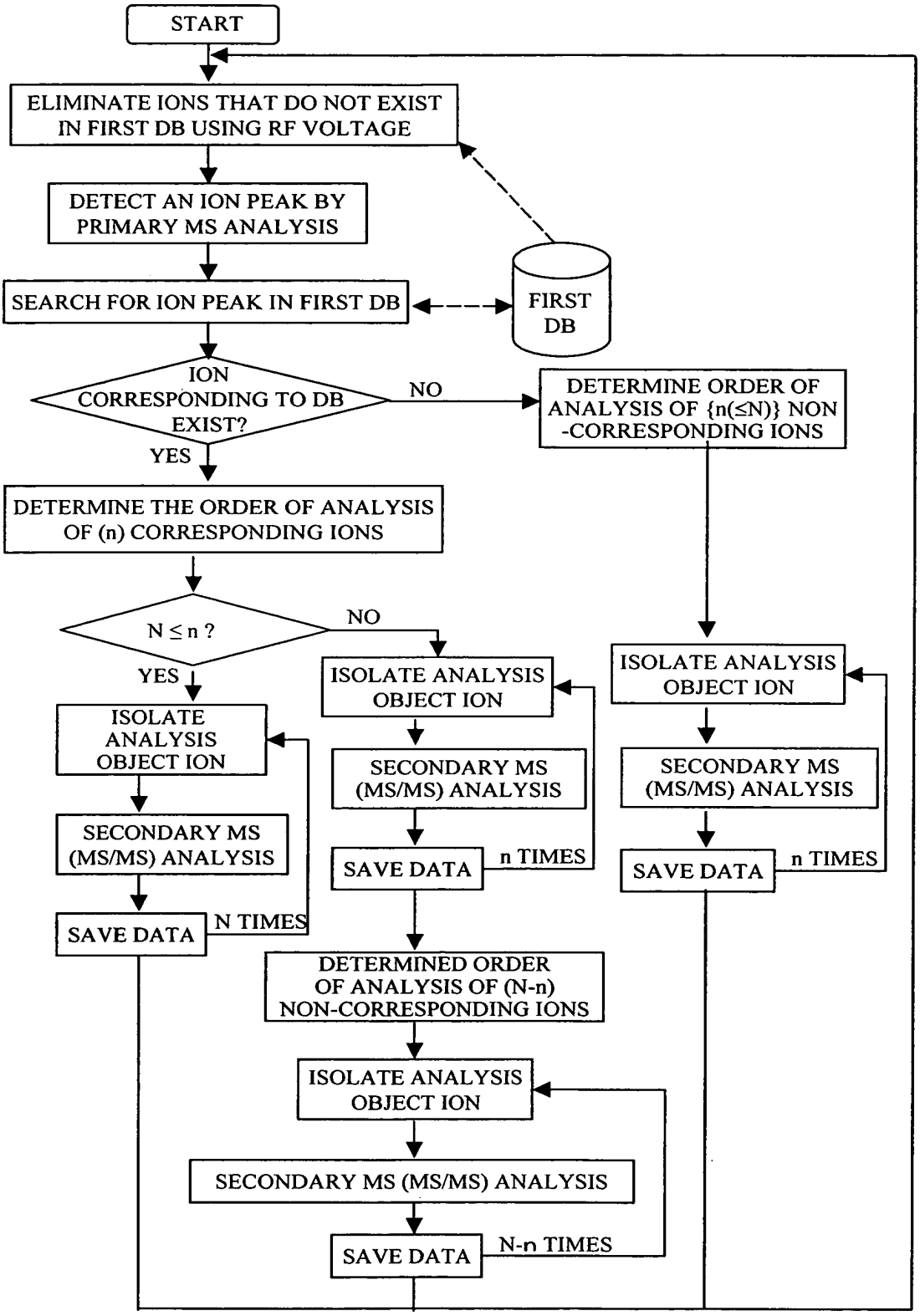

START
ELIMINATE IONS THAT DO NOT EXIST IN FIRST DB USING RF VOLTAGE
DETECT AN ION PEAK BY PRIMARY MS ANALYSIS
SEARCH FOR ION PEAK IN FIRST DB
FIRST DB
ION CORRESPONDING TO DB EXIST?
NO
YES
DETERMINE ORDER OF ANALYSIS OF {n(≤N)} NON -CORRESPONDING IONS
DETERMINE THE ORDER OF ANALYSIS OF (n) CORRESPONDING IONS
N ≤ n ?
NO
YES
ISOLATE ANALYSIS OBJECT ION
SECONDARY MS (MS/MS) ANALYSIS
SAVE DATA
N TIMES
ISOLATE ANALYSIS OBJECT ION
SECONDARY MS (MS/MS) ANALYSIS
SAVE DATA
n TIMES
ISOLATE ANALYSIS OBJECT ION
SECONDARY MS (MS/MS) ANALYSIS
SAVE DATA
n TIMES
DETERMINED ORDER OF ANALYSIS OF (N-n) NON-CORRESPONDING IONS
ISOLATE ANALYSIS OBJECT ION
SECONDARY MS (MS/MS) ANALYSIS
SAVE DATA
N-n TIMES

FIG. 49

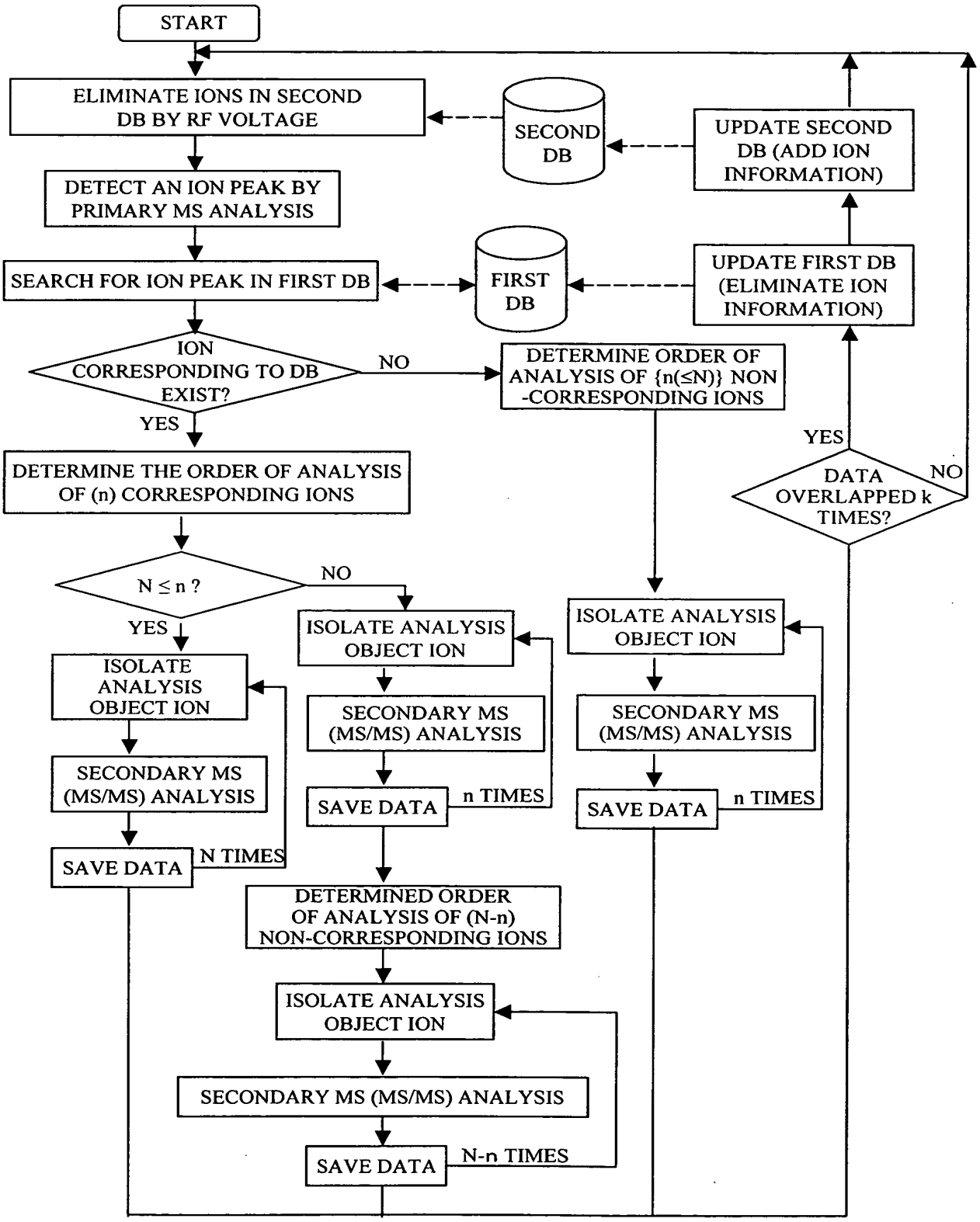

START
ELIMINATE IONS IN SECOND DB BY RF VOLTAGE
SECOND DB
UPDATE SECOND DB (ADD ION INFORMATION)
DETECT AN ION PEAK BY PRIMARY MS ANALYSIS
SEARCH FOR ION PEAK IN FIRST DB
FIRST DB
UPDATE FIRST DB (ELIMINATE ION INFORMATION)
ION CORRESPONDING TO DB EXIST?
NO
DETERMINE ORDER OF ANALYSIS OF {n(≤N)} NON -CORRESPONDING IONS
YES
DETERMINE THE ORDER OF ANALYSIS OF (n) CORRESPONDING IONS
YES
DATA OVERLAPPED k TIMES?
NO
N ≤ n ?
NO
YES
ISOLATE ANALYSIS OBJECT ION
ISOLATE ANALYSIS OBJECT ION
ISOLATE ANALYSIS OBJECT ION
SECONDARY MS (MS/MS) ANALYSIS
SECONDARY MS (MS/MS) ANALYSIS
SECONDARY MS (MS/MS) ANALYSIS
SAVE DATA
n TIMES
SAVE DATA
n TIMES
SAVE DATA
N TIMES
DETERMINED ORDER OF ANALYSIS OF (N-n) NON-CORRESPONDING IONS
ISOLATE ANALYSIS OBJECT ION
SECONDARY MS (MS/MS) ANALYSIS
SAVE DATA
N-n TIMES

FIG. 50

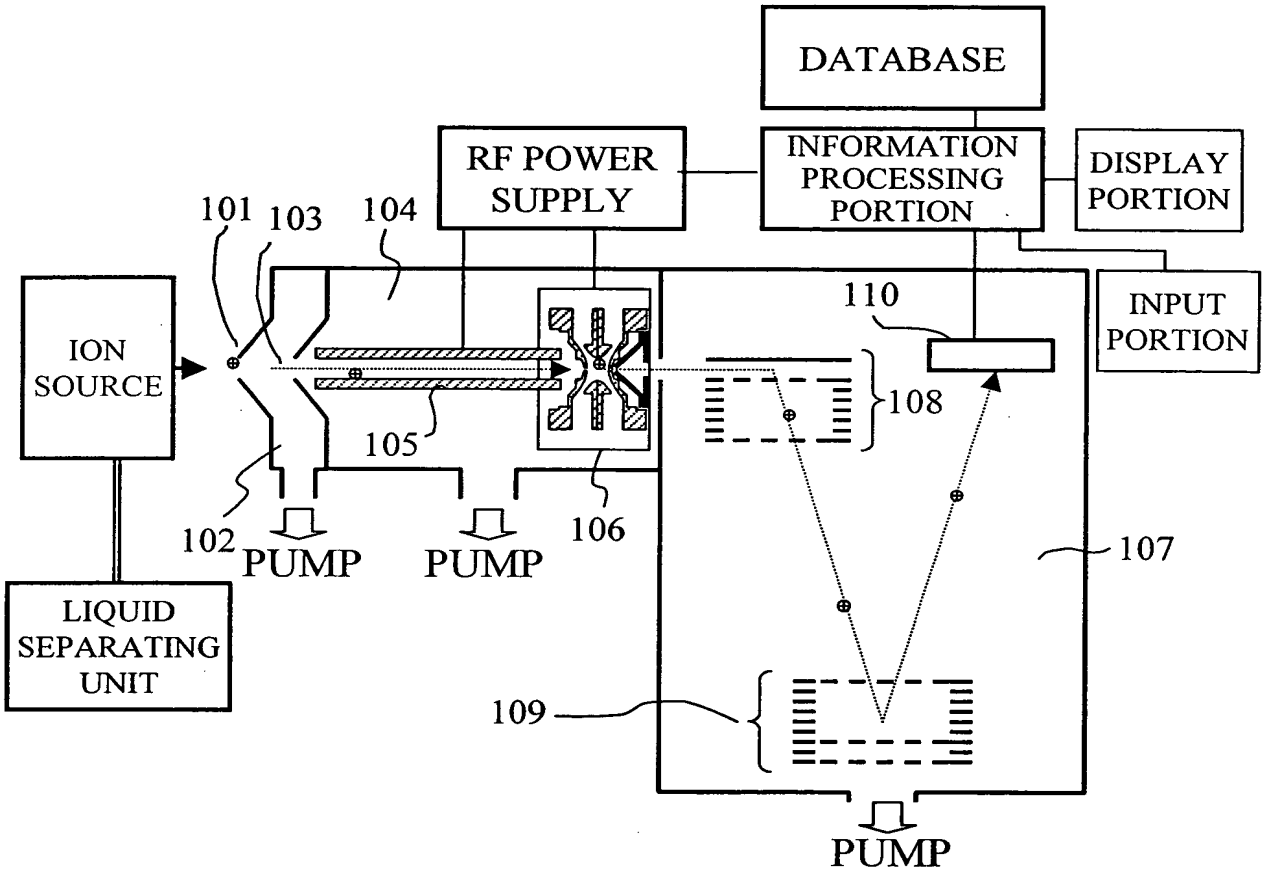

DATABASE
RF POWER SUPPLY
INFORMATION PROCESSING PORTION
DISPLAY PORTION
INPUT PORTION
ION SOURCE
LIQUID SEPARATING UNIT
101
103
104
105
106
107
108
109
110
102
PUMP
PUMP
PUMP

FIG. 51

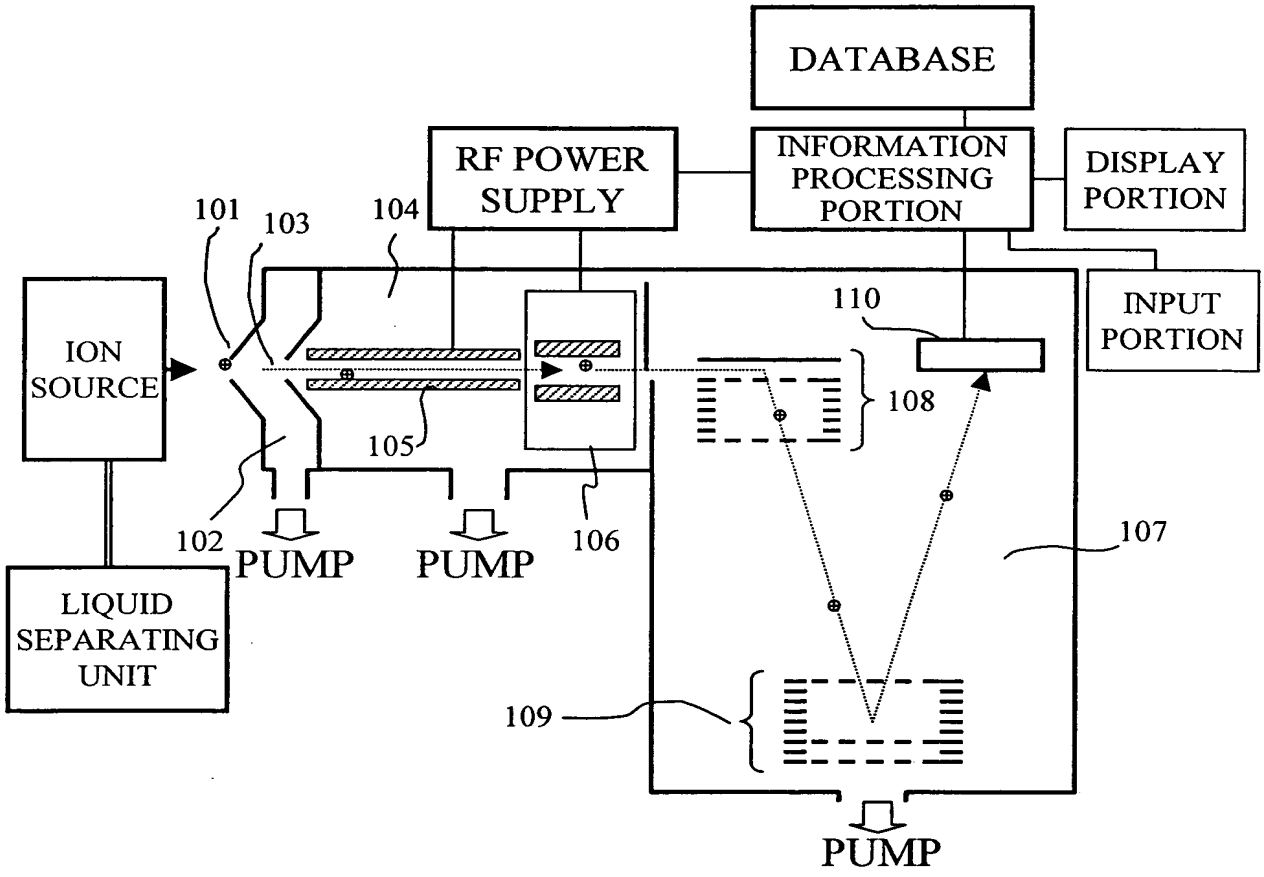
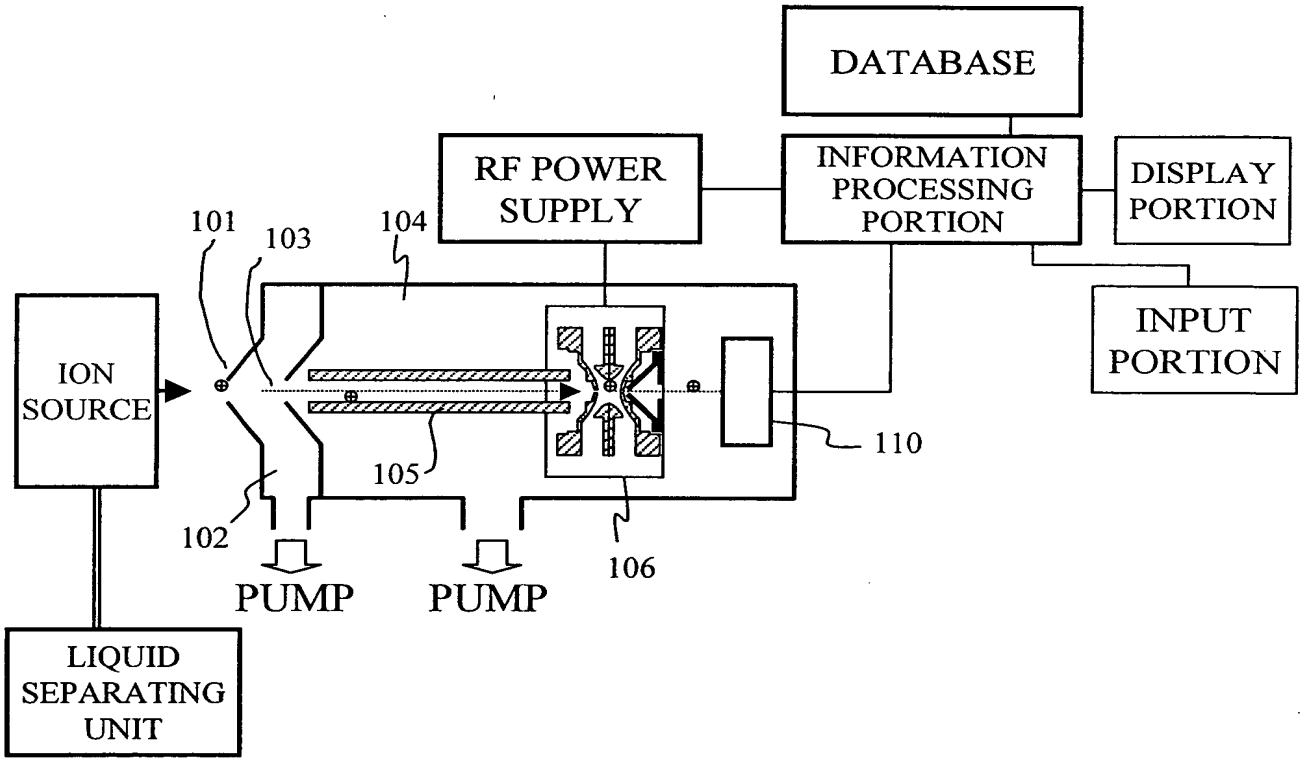

DATABASE
RF POWER SUPPLY
INFORMATION PROCESSING PORTION
DISPLAY PORTION
INPUT PORTION
ION SOURCE
LIQUID SEPARATING UNIT
PUMP
PUMP
PUMP
101
102
103
104
105
106
107
108
109
110

FIG. 52


DATABASE
RF POWER SUPPLY
INFORMATION PROCESSING PORTION
DISPLAY PORTION
INPUT PORTION
ION SOURCE
101
103
104
105
102
106
110
PUMP
PUMP
LIQUID SEPARATING UNIT

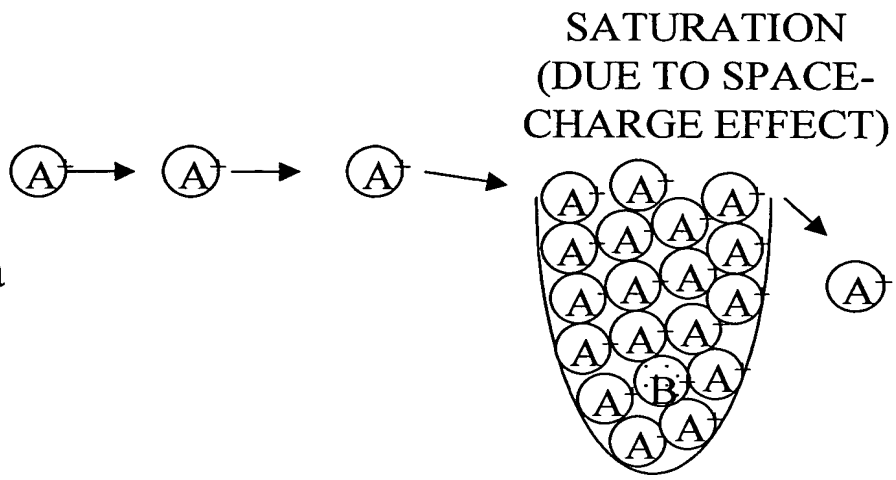


FIG. 53 a

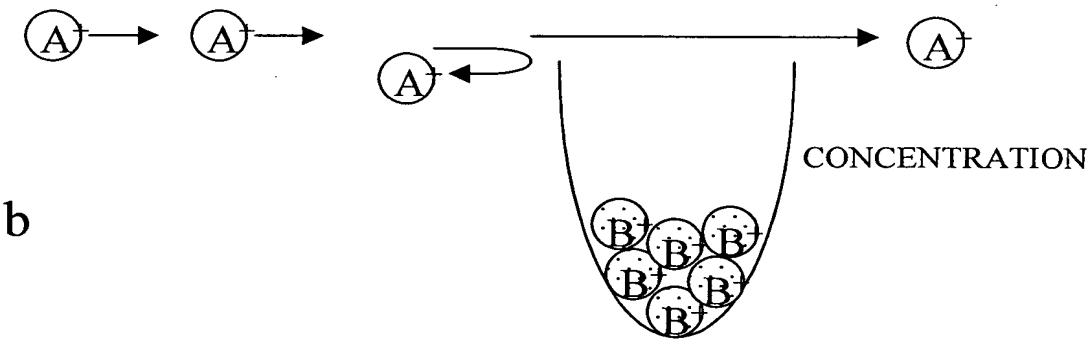


FIG. 53 b

FIG. 54

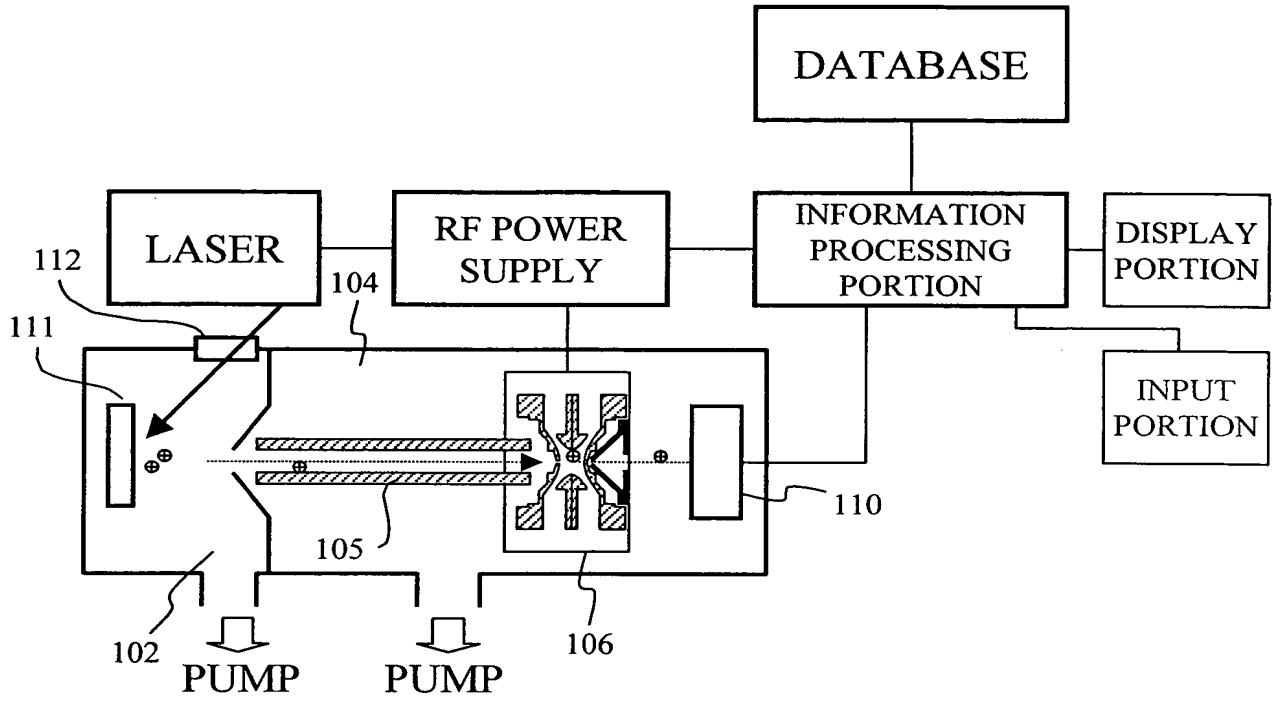

DATABASE
LASER
RF POWER SUPPLY
INFORMATION PROCESSING PORTION
DISPLAY PORTION
INPUT PORTION
112
104
111
110
105
102
106
PUMP
PUMP

FIG. 55

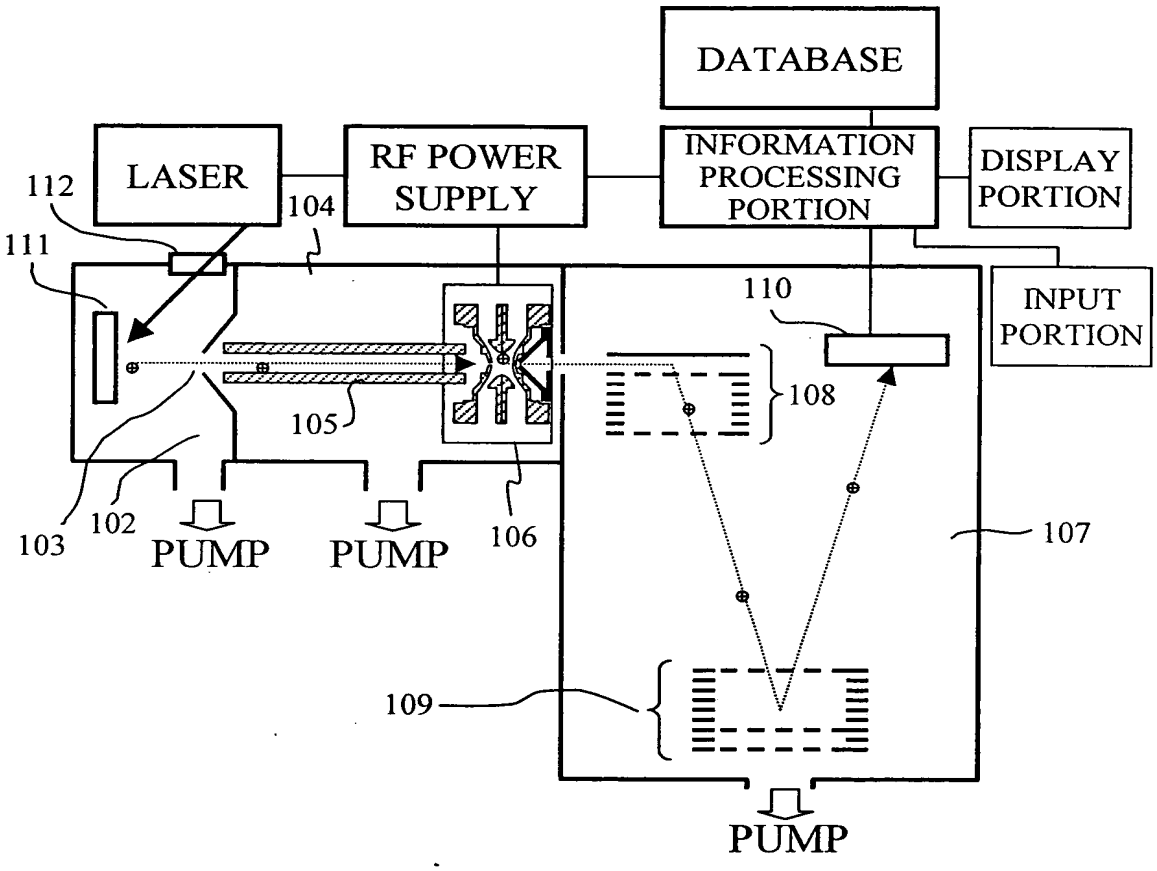

DATABASE
LASER
RF POWER SUPPLY
INFORMATION PROCESSING PORTION
DISPLAY PORTION
INPUT PORTION
112
104
111
110
108
105
103
102
PUMP
PUMP
106
107
109
PUMP

FIG. 56

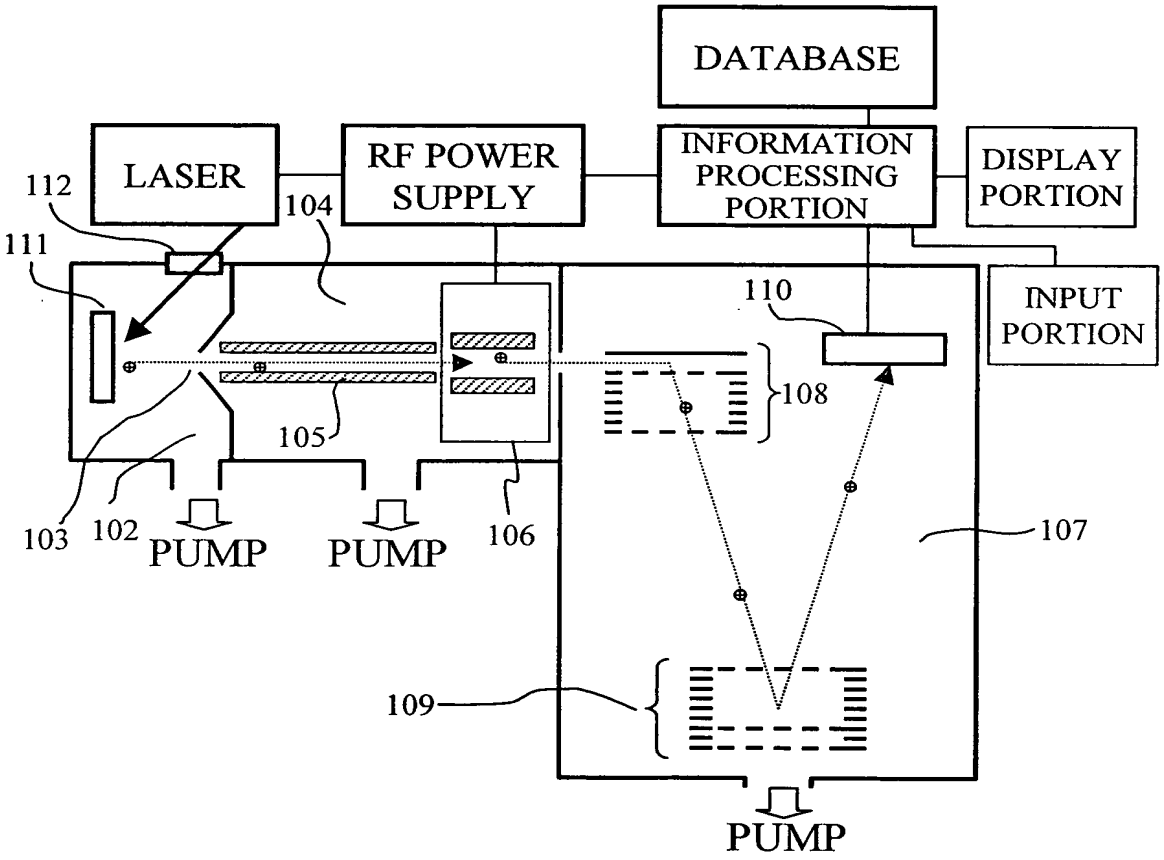

DATABASE
LASER
RF POWER SUPPLY
INFORMATION PROCESSING PORTION
DISPLAY PORTION
INPUT PORTION
112
104
111
110
108
105
103
102
PUMP
PUMP
106
107
109
PUMP

FIG. 57

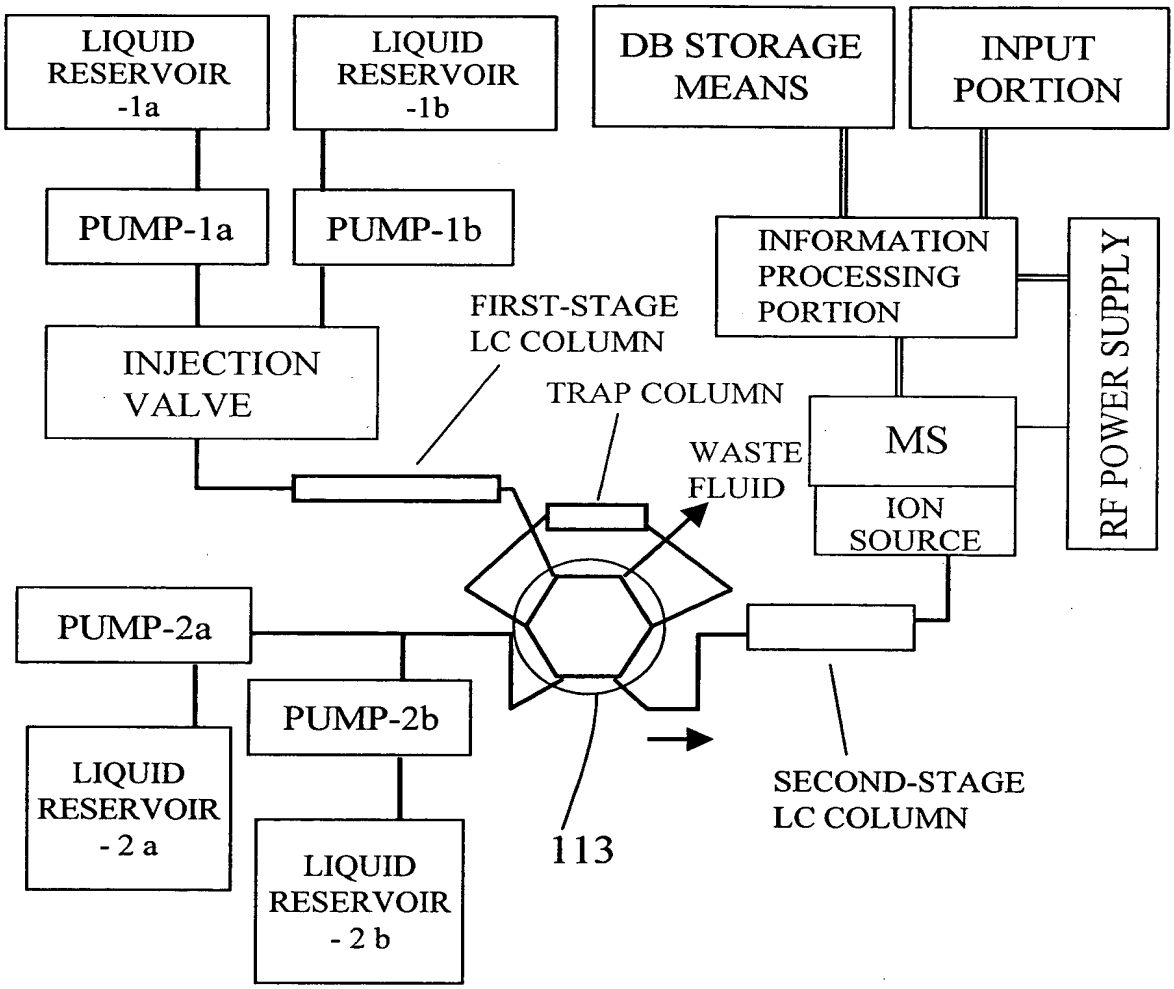

LIQUID RESERVOIR -1a
LIQUID RESERVOIR -1b
DB STORAGE MEANS
INPUT PORTION
PUMP-1a
PUMP-1b
INFORMATION PROCESSING PORTION
RF POWER SUPPLY
FIRST-STAGE LC COLUMN
INJECTION VALVE
TRAP COLUMN
WASTE FLUID
MS
ION SOURCE
PUMP-2a
PUMP-2b
LIQUID RESERVOIR - 2 a
LIQUID RESERVOIR - 2 b
113
SECOND-STAGE LC COLUMN

FIG. 58

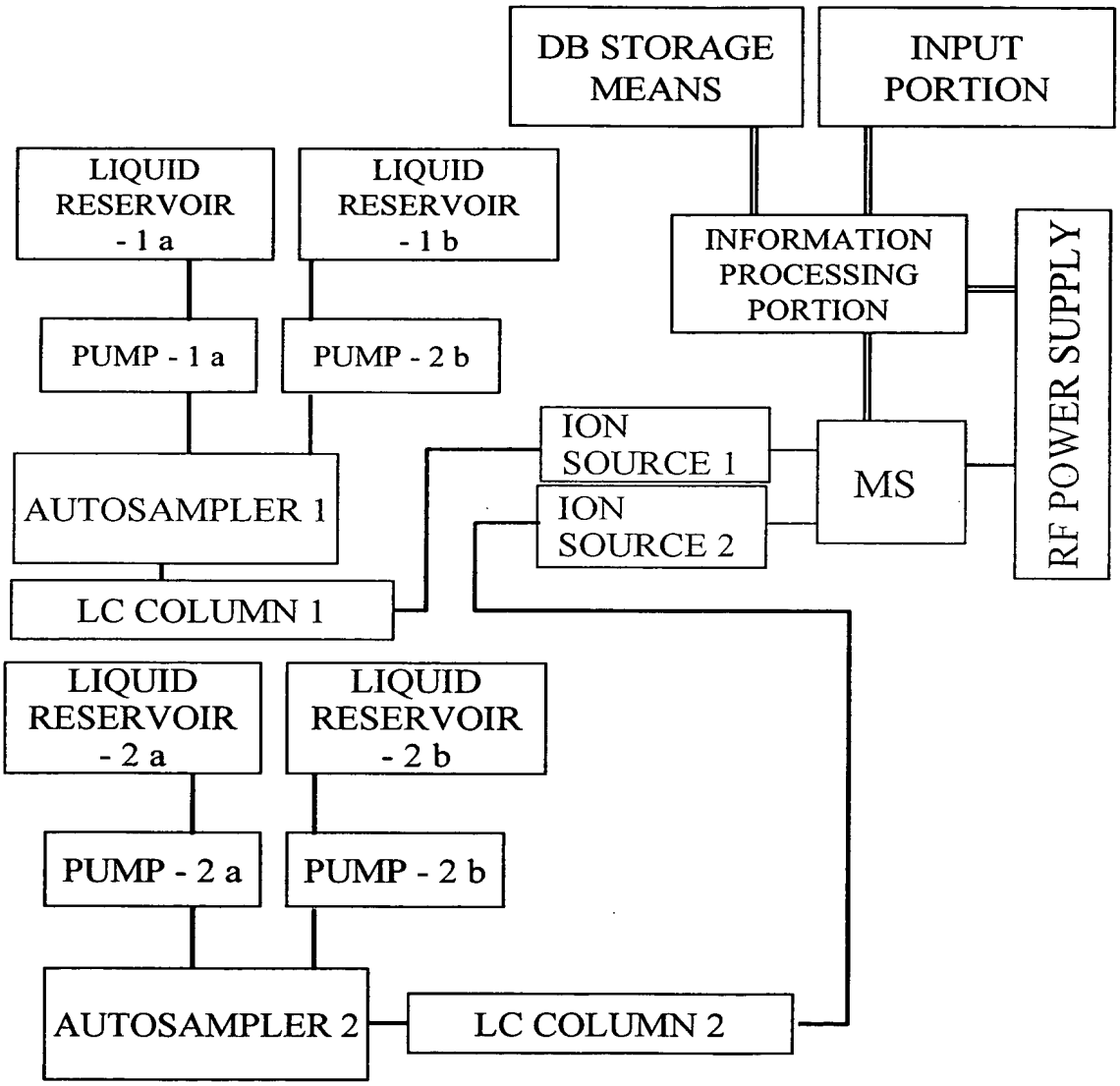

DB STORAGE MEANS
INPUT PORTION
LIQUID RESERVOIR - 1 a
LIQUID RESERVOIR - 1 b
INFORMATION PROCESSING PORTION
RF POWER SUPPLY
PUMP - 1 a
PUMP - 2 b
ION SOURCE 1
MS
AUTOSAMPLER 1
ION SOURCE 2
LC COLUMN 1
LIQUID RESERVOIR - 2 a
LIQUID RESERVOIR - 2 b
PUMP - 2 a
PUMP - 2 b
AUTOSAMPLER 2
LC COLUMN 2

FIG. 59

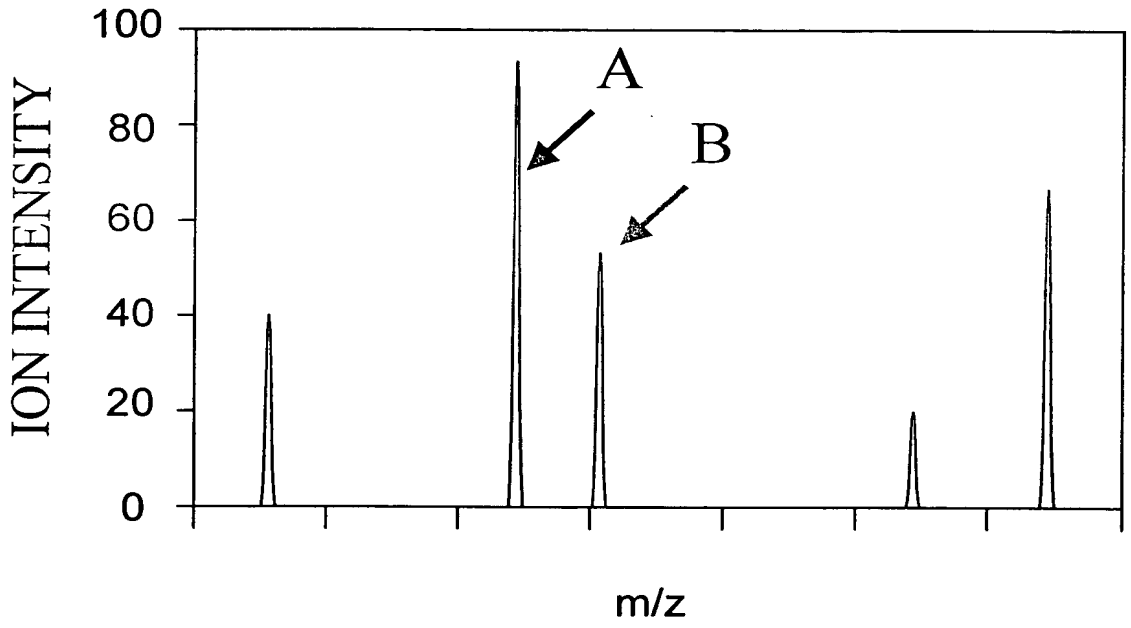
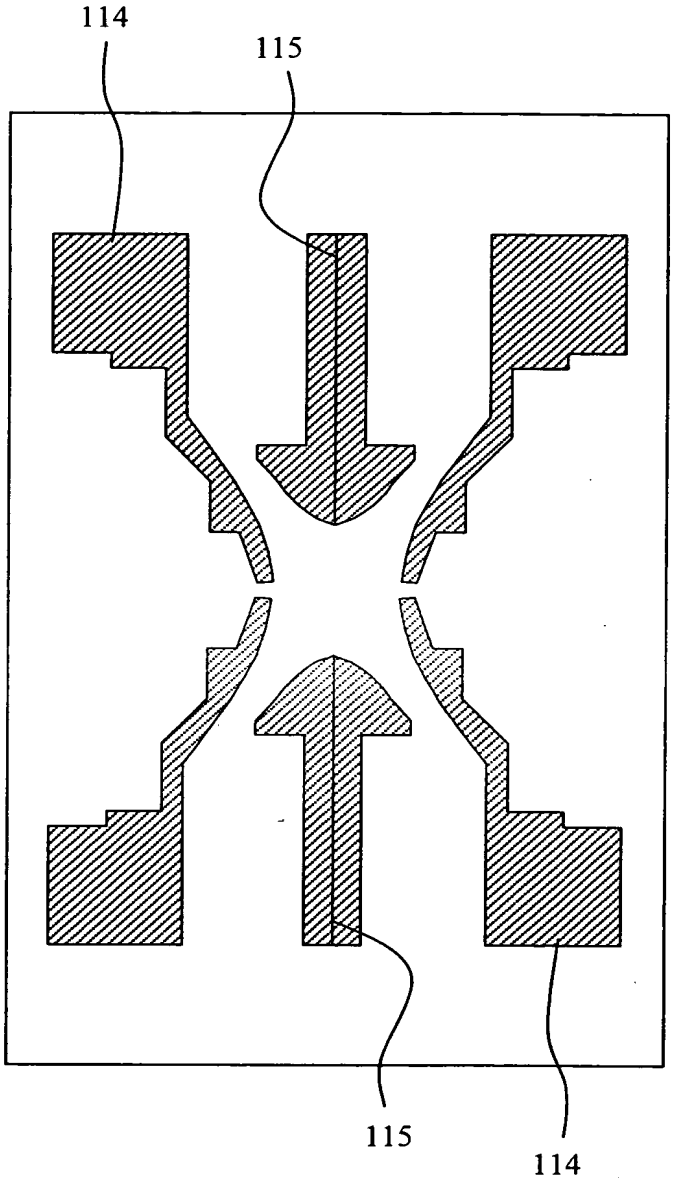


FIG. 60



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